Search history

10/27/2006

```
=> d his full

     (FILE 'HOME' ENTERED AT 12:40:28 ON 26 OCT 2006)

     FILE 'CAPLUS' ENTERED AT 12:40:34 ON 26 OCT 2006
                E US2005-526780/APPS
L1            1 SEA ABB=ON  PLU=ON  US2005-526780/AP
                D SCA
                SEL RN

     FILE 'REGISTRY' ENTERED AT 12:41:00 ON 26 OCT 2006
L2            9 SEA ABB=ON  PLU=ON  (24201-13-6/BI OR 33996-28-0/BI OR
                33996-30-4/BI OR 672285-79-9/BI OR 672285-80-2/BI OR 672285-81-
                3/BI OR 672285-82-4/BI OR 672285-83-5/BI OR 672285-84-6/BI)
                D SCA

     FILE 'STNGUIDE' ENTERED AT 12:44:26 ON 26 OCT 2006

     FILE 'REGISTRY' ENTERED AT 12:53:56 ON 26 OCT 2006
L3              STRUCTURE UPLOADED
L4            4 SEA SSS SAM L3
                D SCA
L5              STRUCTURE UPLOADED
L6            4 SEA SSS SAM L5
L7           47 SEA SSS FUL L5
                SAVE TEMP L7 SPI780STR7L/A

     FILE 'CAPLUS' ENTERED AT 12:59:24 ON 26 OCT 2006
L8           18 SEA ABB=ON  PLU=ON  L7
L9            1 SEA ABB=ON  PLU=ON  L8 AND L1
                D SCA
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 13:01:16 ON 26 OCT 2006
L10           2 SEA ABB=ON  PLU=ON  (672285-79-9/BI OR 672285-84-6/BI)

     FILE 'REGISTRY' ENTERED AT 13:01:41 ON 26 OCT 2006
                D IDE L10 1-2

     FILE 'CAPLUS' ENTERED AT 13:03:06 ON 26 OCT 2006
                D SCA L8
L11      105205 SEA ABB=ON  PLU=ON  ?STOMACH?/BI
L12       42051 SEA ABB=ON  PLU=ON  ?MOTIL?/BI
L13        4188 SEA ABB=ON  PLU=ON  ?PERISTAL?/BI
L14      249583 SEA ABB=ON  PLU=ON  ?DIGEST?/BI
L*** DEL 199220 S ?INTESTIN?
L15      288318 SEA ABB=ON  PLU=ON  ?INTESTIN?/BI
L16       43191 SEA ABB=ON  PLU=ON  (5HT OR 5 HT?)/BI
L17       77545 SEA ABB=ON  PLU=ON  ?SEROTONIN?/BI
L18       22550 SEA ABB=ON  PLU=ON  ?ILEUM?/BI
L19       18576 SEA ABB=ON  PLU=ON  ?JEJUN?/BI
L20       31539 SEA ABB=ON  PLU=ON  ?DUODEN?/BI
L21      139482 SEA ABB=ON  PLU=ON  TRACT#/BI
L22      171670 SEA ABB=ON  PLU=ON  ?GASTR?/BI
L23          12 SEA ABB=ON  PLU=ON  L8 AND (L11 OR L12 OR L13 OR L14 OR L15 OR
                L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22)
L24         162 SEA ABB=ON  PLU=ON  KITAJIMA A?/AU
L25           3 SEA ABB=ON  PLU=ON  AKIHIKO K?/AU
L26           5 SEA ABB=ON  PLU=ON  KAMODA O?/AU
L27          22 SEA ABB=ON  PLU=ON  OSAMU K?/AU
```

```
              E KAMODA/AU
L28             6 SEA ABB=ON  PLU=ON  OHSAKO A?/AU
L29             2 SEA ABB=ON  PLU=ON  AKIHIRO O?/AU
L30           574 SEA ABB=ON  PLU=ON  YANAGI T?/AU
L31             1 SEA ABB=ON  PLU=ON  TOSHIHARU Y?/AU
L32           165 SEA ABB=ON  PLU=ON  (L24 OR L25)
L33            27 SEA ABB=ON  PLU=ON  (L26 OR L27)
L34             8 SEA ABB=ON  PLU=ON  (L28 OR L29)
L35           575 SEA ABB=ON  PLU=ON  (L30 OR L31)
L36             1 SEA ABB=ON  PLU=ON  L32 AND (L33 OR L34 OR L35)
L37             5 SEA ABB=ON  PLU=ON  L33 AND (L34 OR L35)
L38             1 SEA ABB=ON  PLU=ON  L34 AND L35
L39             5 SEA ABB=ON  PLU=ON  (L36 OR L37 OR L38)
L40             3 SEA ABB=ON  PLU=ON  (L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR
                  L30 OR L31) AND (L23 OR L8)

    FILE 'MEDLINE' ENTERED AT 13:14:46 ON 26 OCT 2006
L41           235 SEA ABB=ON  PLU=ON  (L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR
                  L30 OR L31)
L42             2 SEA ABB=ON  PLU=ON  (L36 OR L37 OR L38)

    FILE 'REGISTRY' ENTERED AT 13:16:02 ON 26 OCT 2006
                  SET SMARTSELECT ON
L43               SEL PLU=ON  L7 1- CHEM :      49 TERMS
                  SET SMARTSELECT OFF

    FILE 'MEDLINE' ENTERED AT 13:16:05 ON 26 OCT 2006
L44             3 SEA ABB=ON  PLU=ON  L43
                  D SCA
                  D TRIAL 1-3
                  D QUE L44
                  D L43
                  D L43 1-49
L45             0 SEA ABB=ON  PLU=ON  FAUC65
L46             5 SEA ABB=ON  PLU=ON  TKS159
                  D TRIAL 1-5
L47       1149902 SEA ABB=ON  PLU=ON  (L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR
                  L17 OR L18 OR L19 OR L20 OR L21 OR L22)
L48             5 SEA ABB=ON  PLU=ON  L47 AND ((L44 OR L45 OR L46))
L49             2 SEA ABB=ON  PLU=ON  L41 AND (L44 OR L46 OR L48)

    FILE 'EMBASE' ENTERED AT 13:20:17 ON 26 OCT 2006
L50           198 SEA ABB=ON  PLU=ON  (L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR
                  L30 OR L31)
L51             2 SEA ABB=ON  PLU=ON  (L36 OR L37 OR L38)

    FILE 'REGISTRY' ENTERED AT 13:20:54 ON 26 OCT 2006
                  SET SMARTSELECT ON
L52               SEL PLU=ON  L7 1- CHEM :      49 TERMS
                  SET SMARTSELECT OFF

    FILE 'EMBASE' ENTERED AT 13:20:56 ON 26 OCT 2006
L53             7 SEA ABB=ON  PLU=ON  L52
L54             4 SEA ABB=ON  PLU=ON  FAUC65 OR TKS159
L55             7 SEA ABB=ON  PLU=ON  (L53 OR L54)
L56             7 SEA ABB=ON  PLU=ON  (L53 OR L54) AND (L11 OR L12 OR L13 OR L14
                  OR L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22)
                  D TRIAL 1-7
L57             2 SEA ABB=ON  PLU=ON  L50 AND (L53 OR L54 OR L56)
```

```
     FILE 'BIOSIS' ENTERED AT 13:25:28 ON 26 OCT 2006
L58          252 SEA ABB=ON  PLU=ON  (L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR
                 L30 OR L31)
L59            4 SEA ABB=ON  PLU=ON  (L36 OR L37 OR L38)

     FILE 'REGISTRY' ENTERED AT 13:25:56 ON 26 OCT 2006
                 SET SMARTSELECT ON
L60              SEL PLU=ON  L7 1- CHEM :       49 TERMS
                 SET SMARTSELECT OFF

     FILE 'BIOSIS' ENTERED AT 13:25:57 ON 26 OCT 2006
L61            3 SEA ABB=ON  PLU=ON  L60
L62            5 SEA ABB=ON  PLU=ON  FAUC65 OR TKS159
L63            2 SEA ABB=ON  PLU=ON  L58 AND (L61 OR L62)

     FILE 'REGISTRY' ENTERED AT 13:27:39 ON 26 OCT 2006
L64            1 SEA ABB=ON  PLU=ON  FAUC 65/CN
L65            1 SEA ABB=ON  PLU=ON  TKS 159/CN
                 D SCA
                 D SCA L64
                 SEL RN L10
                 SEL RN L64
                 SEL RN L65
L66            1 SEA ABB=ON  PLU=ON  (672285-79-9/CRN OR 672285-84-6/CRN OR
                 627529-76-4/CRN OR 142228-17-9/CRN)
                 D SCA
                 D IDE L64
                 D IDE L65
                 D IDE L66
                 D STAT QUE L7
L67            4 SEA ABB=ON  PLU=ON  L65 OR L66 OR L10
                 D SCA

     FILE 'USPATFULL, USPAT2' ENTERED AT 13:39:42 ON 26 OCT 2006
L68            3 SEA ABB=ON  PLU=ON  L67
                 D SCA
L69            4 SEA ABB=ON  PLU=ON  L7
L70       308291 SEA ABB=ON  PLU=ON  (L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR
                 L17 OR L18 OR L19 OR L20 OR L21 OR L22)
L71            3 SEA ABB=ON  PLU=ON  L69 AND L70
L72          183 SEA ABB=ON  PLU=ON  L41
L73            7 SEA ABB=ON  PLU=ON  L42
L74            1 SEA ABB=ON  PLU=ON  L72 AND (L69 OR L71)

     FILE 'STNGUIDE' ENTERED AT 13:42:37 ON 26 OCT 2006

     FILE 'REGISTRY' ENTERED AT 13:45:53 ON 26 OCT 2006
                 D STAT QUE L7

     FILE 'CAPLUS' ENTERED AT 13:45:54 ON 26 OCT 2006
                 D QUE NOS L39
                 D QUE NOS L40
L75            6 SEA ABB=ON  PLU=ON  L39 OR L40

     FILE 'MEDLINE' ENTERED AT 13:45:58 ON 26 OCT 2006
                 D QUE NOS L42
                 D QUE NOS L49
L76            3 SEA ABB=ON  PLU=ON  L42 OR L49

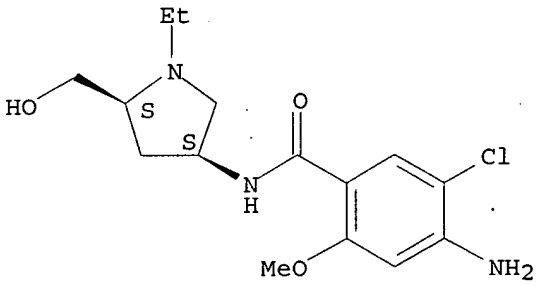
     FILE 'EMBASE' ENTERED AT 13:46:01 ON 26 OCT 2006
```

12 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d ide L66

L66 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
RN 142347-77-1 REGISTRY
ED Entered STN: 10 Jul 1992
CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride, (3S-cis)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C15 H22 Cl N3 O3 . Cl H
SR CA
LC STN Files: CA, CAPLUS, PROUSDDR, USPATFULL
CRN (142228-17-9)

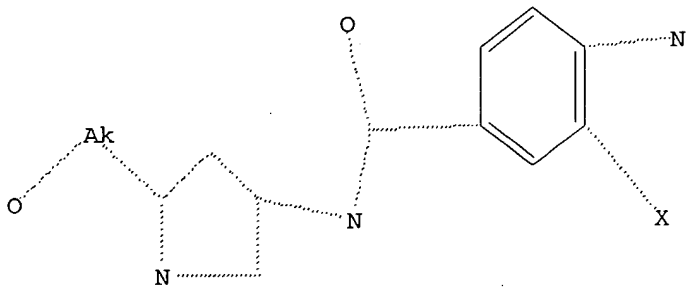
Absolute stereochemistry.



● HCl

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> => d stat que L7
L5 STR



Structure attributes must be viewed using STN Express query preparation.
L7 47 SEA FILE=REGISTRY SSS FUL L5

100.0% PROCESSED 11082 ITERATIONS 47 ANSWERS
SEARCH TIME: 00.00.01

```
=> => file registry
FILE 'REGISTRY' ENTERED AT 13:45:53 ON 26 OCT 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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provided by InfoChem.

STRUCTURE FILE UPDATES:   25 OCT 2006  HIGHEST RN 911284-77-0
DICTIONARY FILE UPDATES:  25 OCT 2006  HIGHEST RN 911284-77-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

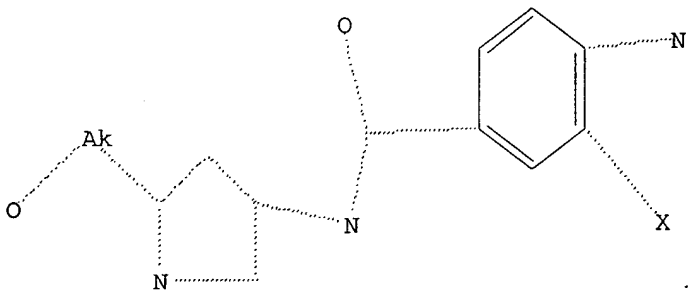
  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

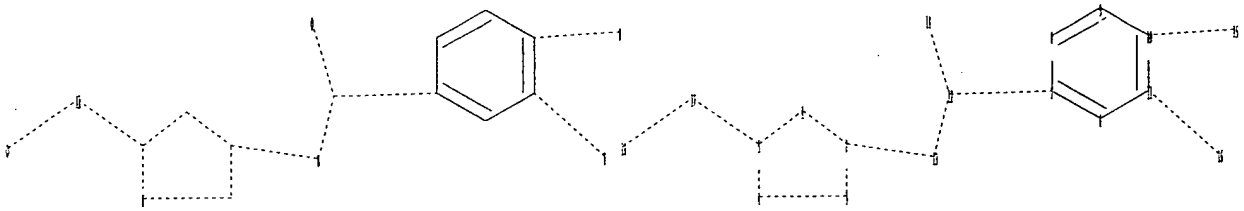
http://www.cas.org/ONLINE/UG/regprops.html

=> d stat que L7

L5                STR
```




```
Structure attributes must be viewed using STN Express query preparation.
Uploading L5.str
```



```
chain nodes :
12  13  14  15  16  17  18
ring nodes :
1  2  3  4  5  6  7  8  9  10  11
```

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE EMBASE
FILE COVERS 1974 TO 26 Oct 2006 (20061026/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 18 October 2006 (20061018/ED)

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 26 Oct 2006 (20061026/PD)
FILE LAST UPDATED: 26 Oct 2006 (20061026/ED)
HIGHEST GRANTED PATENT NUMBER: US7127745
HIGHEST APPLICATION PUBLICATION NUMBER: US2006242744
CA INDEXING IS CURRENT THROUGH 24 Oct 2006 (20061024/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 26 Oct 2006 (20061026/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2006

FILE USPAT2

FILE COVERS 2001 TO PUBLICATION DATE: 26 Oct 2006 (20061026/PD)
FILE LAST UPDATED: 26 Oct 2006 (20061026/ED)
HIGHEST GRANTED PATENT NUMBER: US2006139723
HIGHEST APPLICATION PUBLICATION NUMBER: US2006242346
CA INDEXING IS CURRENT THROUGH 26 Oct 2006 (20061026/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 26 Oct 2006 (20061026/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2006

```
=> file registry
FILE 'REGISTRY' ENTERED AT 13:01:41 ON 26 OCT 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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STRUCTURE FILE UPDATES:   25 OCT 2006  HIGHEST RN 911284-77-0
DICTIONARY FILE UPDATES:  25 OCT 2006  HIGHEST RN 911284-77-0

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TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

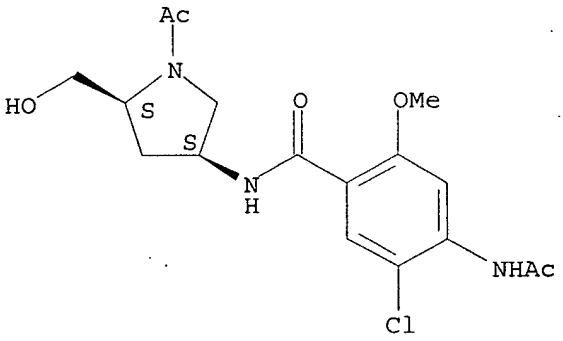
REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> d ide L10 1-2

L10  ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   672285-84-6  REGISTRY
ED   Entered STN:  07 Apr 2004
CN   Benzamide, 4-(acetylamino)-N-[(3S,5S)-1-acetyl-5-(hydroxymethyl)-3-
     pyrrolidinyl]-5-chloro-2-methoxy-  (9CI)  (CA INDEX NAME)
FS   STEREOSEARCH
MF   C17 H22 Cl N3 O5
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.
```

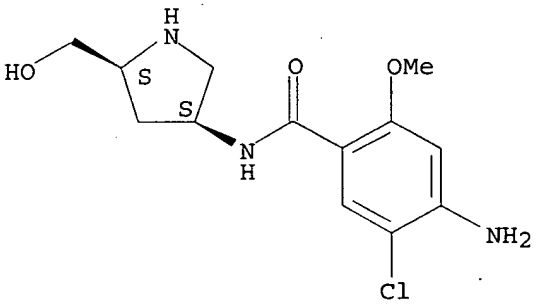



```
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

              1 REFERENCES IN FILE CA (1907 TO DATE)
              1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
```

L10 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2006 ACS on STN
RN ***672285-79-9*** REGISTRY
ED Entered STN: 07 Apr 2004
CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C13 H18 Cl N3 O3 . Cl H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
CRN (765269-94-1)

Absolute stereochemistry.



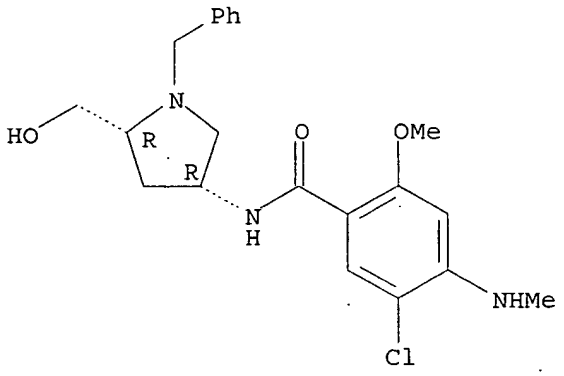
● HCl

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> => => d ide L64

L64 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
RN 627529-76-4 REGISTRY
ED Entered STN: 19 Dec 2003
CN Benzamide, 5-chloro-N-[(3R,5R)-5-(hydroxymethyl)-1-(phenylmethyl)-3-pyrrolidinyl]-2-methoxy-4-(methylamino)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN ***FAUC 65***
FS STEREOSEARCH
MF C21 H26 Cl N3 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry. Rotation (-).



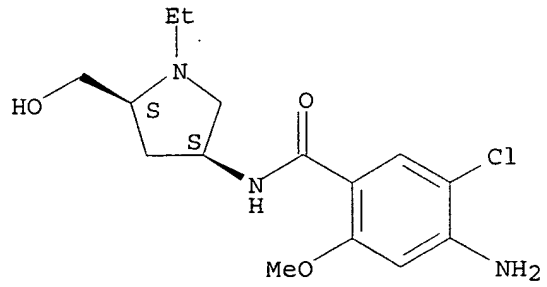
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d ide L65

L65 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
RN 142228-17-9 REGISTRY
ED Entered STN: 03 Jul 1992
CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, (3S-cis)-
OTHER NAMES:
CN ***TKS 159***
FS STEREOSEARCH
MF C15 H22 Cl N3 O3
CI COM
SR CA
LC STN Files: ADISINSIGHT, BIOSIS, CA, CAPLUS, PROUSDDR, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

12 REFERENCES IN FILE CA (1907 TO DATE)

```
                D QUE NOS L51
                D QUE NOS L57
L77           3 SEA ABB=ON  PLU=ON  L51 OR L57

     FILE 'BIOSIS' ENTERED AT 13:46:04 ON 26 OCT 2006
                D QUE NOS L59
                D QUE NOS L63
L78           5 SEA ABB=ON  PLU=ON  L59 OR L63

     FILE 'USPATFULL, USPAT2' ENTERED AT 13:46:07 ON 26 OCT 2006
                D QUE NOS L73
                D QUE NOS L74
L79           7 SEA ABB=ON  PLU=ON  L73 OR L74

     FILE 'STNGUIDE' ENTERED AT 13:46:29 ON 26 OCT 2006

     FILE 'CAPLUS, MEDLINE, EMBASE, BIOSIS, USPATFULL, USPAT2' ENTERED AT
     13:46:50 ON 26 OCT 2006
L80          12 DUP REM L75 L76 L77 L78 L79 (12 DUPLICATES REMOVED)
                    ANSWERS '1-6' FROM FILE CAPLUS
                    ANSWERS '7-9' FROM FILE BIOSIS
                    ANSWERS '10-12' FROM FILE USPATFULL
                D IBIB ABS HITIND HITSTR L80 1-6
                D IALL L80 7-9
                D IBIB ABS KWIC HITSTR L80 10-12

     FILE 'REGISTRY' ENTERED AT 13:51:05 ON 26 OCT 2006
                D STAT QUE L7

     FILE 'CAPLUS' ENTERED AT 13:51:07 ON 26 OCT 2006
                D QUE NOS L8
                D QUE NOS L23
L81          15 SEA ABB=ON  PLU=ON  (L8 OR L23) NOT L75

     FILE 'MEDLINE' ENTERED AT 13:51:10 ON 26 OCT 2006
                D QUE NOS L44
                D QUE NOS L46
                D QUE NOS L48
L82           3 SEA ABB=ON  PLU=ON  (L44 OR L46 OR L48) NOT L76

     FILE 'EMBASE' ENTERED AT 13:51:14 ON 26 OCT 2006
                D QUE NOS L53
                D QUE NOS L54
                D QUE NOS L56
L83           5 SEA ABB=ON  PLU=ON  (L53 OR L54 OR L56) NOT L77

     FILE 'BIOSIS' ENTERED AT 13:51:18 ON 26 OCT 2006
                D QUE NOS L61
                D QUE NOS L62
L84           3 SEA ABB=ON  PLU=ON  (L61 OR L62) NOT L78

     FILE 'USPATFULL, USPAT2' ENTERED AT 13:51:21 ON 26 OCT 2006
                D QUE NOS L69
                D QUE NOS L71
L85           3 SEA ABB=ON  PLU=ON  (L69 OR L71) NOT L79

     FILE 'CAPLUS, MEDLINE, EMBASE, BIOSIS, USPATFULL' ENTERED AT 13:53:56 ON
     26 OCT 2006
L86          22 DUP REM L81 L82 L83 L84 L85 (7 DUPLICATES REMOVED)
                    ANSWERS '1-15' FROM FILE CAPLUS
```

=> => file registry
FILE 'REGISTRY' ENTERED AT 13:45:53 ON 26 OCT 2006

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 25 OCT 2006 HIGHEST RN 911284-77-0
DICTIONARY FILE UPDATES: 25 OCT 2006 HIGHEST RN 911284-77-0

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TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

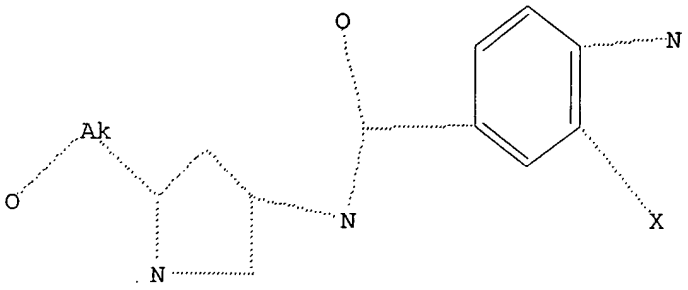
Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

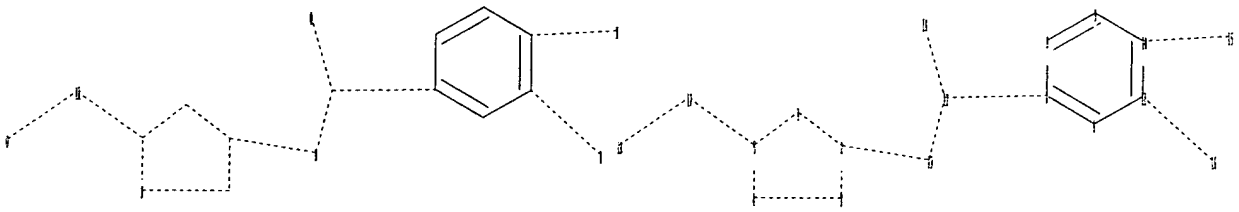
http://www.cas.org/ONLINE/UG/regprops.html

=> d stat que L7

L5 STR



Structure attributes must be viewed using STN Express query preparation.
Uploading L5.str



chain nodes :
12 13 14 15 16 17 18
ring nodes :
1 2 3 4 5 6 7 8 9 10 11

chain bonds :
2-13 5-17 7-12 10-15 11-16 12-13 12-14 17-18
ring bonds :
1-2 1-5 2-3 3-4 4-5 6-7 6-11 7-8 8-9 9-10 10-11
exact/norm bonds :
1-2 1-5 2-3 2-13 3-4 4-5 5-17 7-12 10-15 11-16 12-13 12-14 17-18
normalized bonds :
6-7 6-11 7-8 8-9 9-10 10-11

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS

L7 47 SEA FILE=REGISTRY SSS FUL L5

100.0% PROCESSED 11082 ITERATIONS 47 ANSWERS
SEARCH TIME: 00.00.01

=> file caplus

FILE 'CAPLUS' ENTERED AT 13:45:54 ON 26 OCT 2006
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AUTHOR SEARCH

FILE COVERS 1907 - 26 Oct 2006 VOL 145 ISS 18
FILE LAST UPDATED: 25 Oct 2006 (20061025/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d que nos L39

L24 162 SEA FILE=CAPLUS ABB=ON PLU=ON KITAJIMA A?/AU
L25 3 SEA FILE=CAPLUS ABB=ON PLU=ON AKIHIKO K?/AU
L26 5 SEA FILE=CAPLUS ABB=ON PLU=ON KAMODA O?/AU
L27 22 SEA FILE=CAPLUS ABB=ON PLU=ON OSAMU K?/AU
L28 6 SEA FILE=CAPLUS ABB=ON PLU=ON OHSAKO A?/AU
L29 2 SEA FILE=CAPLUS ABB=ON PLU=ON AKIHIRO O?/AU
L30 574 SEA FILE=CAPLUS ABB=ON PLU=ON YANAGI T?/AU

```
L31           1 SEA FILE=CAPLUS ABB=ON  PLU=ON  TOSHIHARU Y?/AU
L32         165 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L24 OR L25)
L33          27 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L26 OR L27)
L34           8 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L28 OR L29)
L35         575 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L30 OR L31)
L36           1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L32 AND (L33 OR L34 OR L35)
L37           5 SEA FILE=CAPLUS ABB=ON  PLU=ON  L33 AND (L34 OR L35)
L38           1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L34 AND L35
L39           5 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L36 OR L37 OR L38)


=> d que nos L40

L5              STR
L7             47 SEA FILE=REGISTRY SSS FUL L5
L8             18 SEA FILE=CAPLUS ABB=ON  PLU=ON  L7
L11        105205 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?STOMACH?/BI
L12         42051 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?MOTIL?/BI
L13          4188 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?PERISTAL?/BI
L14        249583 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?DIGEST?/BI
L15        288318 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?INTESTIN?/BI
L16         43191 SEA FILE=CAPLUS ABB=ON  PLU=ON  (5HT OR 5 HT?)/BI
L17         77545 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?SEROTONIN?/BI
L18         22550 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?ILEUM?/BI
L19         18576 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?JEJUN?/BI
L20         31539 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?DUODEN?/BI
L21        139482 SEA FILE=CAPLUS ABB=ON  PLU=ON  TRACT#/BI
L22        171670 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?GASTR?/BI
L23            12 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND (L11 OR L12 OR L13 OR
                  L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22)
L24           162 SEA FILE=CAPLUS ABB=ON  PLU=ON  KITAJIMA A?/AU
L25             3 SEA FILE=CAPLUS ABB=ON  PLU=ON  AKIHIKO K?/AU
L26             5 SEA FILE=CAPLUS ABB=ON  PLU=ON  KAMODA O?/AU
L27            22 SEA FILE=CAPLUS ABB=ON  PLU=ON  OSAMU K?/AU
L28             6 SEA FILE=CAPLUS ABB=ON  PLU=ON  OHSAKO A?/AU
L29             2 SEA FILE=CAPLUS ABB=ON  PLU=ON  AKIHIRO O?/AU
L30           574 SEA FILE=CAPLUS ABB=ON  PLU=ON  YANAGI T?/AU
L31             1 SEA FILE=CAPLUS ABB=ON  PLU=ON  TOSHIHARU Y?/AU
L40             3 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L24 OR L25 OR L26 OR L27 OR
                  L28 OR L29 OR L30 OR L31) AND (L23 OR L8)


=> s L39 or L40

L75             6 L39 OR L40

=> file medline

FILE 'MEDLINE' ENTERED AT 13:45:58 ON 26 OCT 2006

 FILE LAST UPDATED: 25 Oct 2006 (20061025/UP).  FILE COVERS 1950 TO DATE.

 On December 11, 2005, the 2006 MeSH terms were loaded.

 The MEDLINE reload for 2006 is now (26 Feb.) available.  For details
 on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
 See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
```

http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> d que nos L42

L24          162 SEA FILE=CAPLUS ABB=ON  PLU=ON  KITAJIMA A?/AU
L25            3 SEA FILE=CAPLUS ABB=ON  PLU=ON  AKIHIKO K?/AU
L26            5 SEA FILE=CAPLUS ABB=ON  PLU=ON  KAMODA O?/AU
L27           22 SEA FILE=CAPLUS ABB=ON  PLU=ON  OSAMU K?/AU
L28            6 SEA FILE=CAPLUS ABB=ON  PLU=ON  OHSAKO A?/AU
L29            2 SEA FILE=CAPLUS ABB=ON  PLU=ON  AKIHIRO O?/AU
L30          574 SEA FILE=CAPLUS ABB=ON  PLU=ON  YANAGI T?/AU
L31            1 SEA FILE=CAPLUS ABB=ON  PLU=ON  TOSHIHARU Y?/AU
L32          165 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L24 OR L25)
L33           27 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L26 OR L27)
L34            8 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L28 OR L29)
L35          575 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L30 OR L31)
L36            1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L32 AND (L33 OR L34 OR L35)
L37            5 SEA FILE=CAPLUS ABB=ON  PLU=ON  L33 AND (L34 OR L35)
L38            1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L34 AND L35
L42            2 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L36 OR L37 OR L38)


=> d que nos L49

L5               STR
L7              47 SEA FILE=REGISTRY SSS FUL L5
L11         105205 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?STOMACH?/BI
L12          42051 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?MOTIL?/BI
L13           4188 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?PERISTAL?/BI
L14         249583 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?DIGEST?/BI
L15         288318 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?INTESTIN?/BI
L16          43191 SEA FILE=CAPLUS ABB=ON  PLU=ON  (5HT OR 5 HT?)/BI
L17          77545 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?SEROTONIN?/BI
L18          22550 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?ILEUM?/BI
L19          18576 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?JEJUN?/BI
L20          31539 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?DUODEN?/BI
L21         139482 SEA FILE=CAPLUS ABB=ON  PLU=ON  TRACT#/BI
L22         171670 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?GASTR?/BI
L24            162 SEA FILE=CAPLUS ABB=ON  PLU=ON  KITAJIMA A?/AU
L25              3 SEA FILE=CAPLUS ABB=ON  PLU=ON  AKIHIKO K?/AU
L26              5 SEA FILE=CAPLUS ABB=ON  PLU=ON  KAMODA O?/AU
L27             22 SEA FILE=CAPLUS ABB=ON  PLU=ON  OSAMU K?/AU
L28              6 SEA FILE=CAPLUS ABB=ON  PLU=ON  OHSAKO A?/AU
L29              2 SEA FILE=CAPLUS ABB=ON  PLU=ON  AKIHIRO O?/AU
L30            574 SEA FILE=CAPLUS ABB=ON  PLU=ON  YANAGI T?/AU
L31              1 SEA FILE=CAPLUS ABB=ON  PLU=ON  TOSHIHARU Y?/AU
L41            235 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L24 OR L25 OR L26 OR L27 OR
                   L28 OR L29 OR L30 OR L31)
L43                SEL  PLU=ON  L7 1- CHEM :       49 TERMS
L44              3 SEA FILE=MEDLINE ABB=ON  PLU=ON  L43
L45              0 SEA FILE=MEDLINE ABB=ON  PLU=ON  FAUC65
```

```
L46           5 SEA FILE=MEDLINE ABB=ON  PLU=ON  TKS159
L47     1149902 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L11 OR L12 OR L13 OR L14 OR
                L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22)
L48           5 SEA FILE=MEDLINE ABB=ON  PLU=ON  L47 AND ((L44 OR L45 OR L46))

L49           2 SEA FILE=MEDLINE ABB=ON  PLU=ON  L41 AND (L44 OR L46 OR L48)


=> s L42 or L49

L76           3 L42 OR L49

=> file embase

FILE 'EMBASE' ENTERED AT 13:46:01 ON 26 OCT 2006
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 FILE COVERS 1974 TO 26 Oct 2006 (20061026/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 EMBASE is now updated daily.  SDI frequency remains weekly (default)
 and biweekly.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que nos L51

L24         162 SEA FILE=CAPLUS ABB=ON  PLU=ON  KITAJIMA A?/AU
L25           3 SEA FILE=CAPLUS ABB=ON  PLU=ON  AKIHIKO K?/AU
L26           5 SEA FILE=CAPLUS ABB=ON  PLU=ON  KAMODA O?/AU
L27          22 SEA FILE=CAPLUS ABB=ON  PLU=ON  OSAMU K?/AU
L28           6 SEA FILE=CAPLUS ABB=ON  PLU=ON  OHSAKO A?/AU
L29           2 SEA FILE=CAPLUS ABB=ON  PLU=ON  AKIHIRO O?/AU
L30         574 SEA FILE=CAPLUS ABB=ON  PLU=ON  YANAGI T?/AU
L31           1 SEA FILE=CAPLUS ABB=ON  PLU=ON  TOSHIHARU Y?/AU
L32         165 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L24 OR L25)
L33          27 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L26 OR L27)
L34           8 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L28 OR L29)
L35         575 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L30 OR L31)
L36           1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L32 AND (L33 OR L34 OR L35)
L37           5 SEA FILE=CAPLUS ABB=ON  PLU=ON  L33 AND (L34 OR L35)
L38           1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L34 AND L35
L51           2 SEA FILE=EMBASE ABB=ON  PLU=ON  (L36 OR L37 OR L38)


=> d que nos L57

L5              STR
L7             47 SEA FILE=REGISTRY SSS FUL L5
L11        105205 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?STOMACH?/BI
L12         42051 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?MOTIL?/BI
L13          4188 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?PERISTAL?/BI
L14        249583 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?DIGEST?/BI
L15        288318 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?INTESTIN?/BI
L16         43191 SEA FILE=CAPLUS ABB=ON  PLU=ON  (5HT OR 5 HT?)/BI
L17         77545 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?SEROTONIN?/BI
L18         22550 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?ILEUM?/BI
L19         18576 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?JEJUN?/BI
```

```
L20         31539 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?DUODEN?/BI
L21        139482 SEA FILE=CAPLUS ABB=ON  PLU=ON  TRACT#/BI
L22        171670 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?GASTR?/BI
L24           162 SEA FILE=CAPLUS ABB=ON  PLU=ON  KITAJIMA A?/AU
L25             3 SEA FILE=CAPLUS ABB=ON  PLU=ON  AKIHIKO K?/AU
L26             5 SEA FILE=CAPLUS ABB=ON  PLU=ON  KAMODA O?/AU
L27            22 SEA FILE=CAPLUS ABB=ON  PLU=ON  OSAMU K?/AU
L28             6 SEA FILE=CAPLUS ABB=ON  PLU=ON  OHSAKO A?/AU
L29             2 SEA FILE=CAPLUS ABB=ON  PLU=ON  AKIHIRO O?/AU
L30           574 SEA FILE=CAPLUS ABB=ON  PLU=ON  YANAGI T?/AU
L31             1 SEA FILE=CAPLUS ABB=ON  PLU=ON  TOSHIHARU Y?/AU
L50           198 SEA FILE=EMBASE ABB=ON  PLU=ON  (L24 OR L25 OR L26 OR L27 OR
                  L28 OR L29 OR L30 OR L31)
L52                 SEL  PLU=ON  L7 1- CHEM :       49 TERMS
L53             7 SEA FILE=EMBASE ABB=ON  PLU=ON  L52
L54             4 SEA FILE=EMBASE ABB=ON  PLU=ON  FAUC65 OR TKS159
L56             7 SEA FILE=EMBASE ABB=ON  PLU=ON  (L53 OR L54) AND (L11 OR L12
                  OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21
                  OR L22)
L57             2 SEA FILE=EMBASE ABB=ON  PLU=ON  L50 AND (L53 OR L54 OR L56)


=> s L51 or L57

L77             3 L51 OR L57

=> file biosis

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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 18 October 2006 (20061018/ED)


=> d que nos L59

L24           162 SEA FILE=CAPLUS ABB=ON  PLU=ON  KITAJIMA A?/AU
L25             3 SEA FILE=CAPLUS ABB=ON  PLU=ON  AKIHIKO K?/AU
L26             5 SEA FILE=CAPLUS ABB=ON  PLU=ON  KAMODA O?/AU
L27            22 SEA FILE=CAPLUS ABB=ON  PLU=ON  OSAMU K?/AU
L28             6 SEA FILE=CAPLUS ABB=ON  PLU=ON  OHSAKO A?/AU
L29             2 SEA FILE=CAPLUS ABB=ON  PLU=ON  AKIHIRO O?/AU
L30           574 SEA FILE=CAPLUS ABB=ON  PLU=ON  YANAGI T?/AU
L31             1 SEA FILE=CAPLUS ABB=ON  PLU=ON  TOSHIHARU Y?/AU
L32           165 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L24 OR L25)
L33            27 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L26 OR L27)
L34             8 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L28 OR L29)
L35           575 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L30 OR L31)
L36             1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L32 AND (L33 OR L34 OR L35)
L37             5 SEA FILE=CAPLUS ABB=ON  PLU=ON  L33 AND (L34 OR L35)
L38             1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L34 AND L35
L59             4 SEA FILE=BIOSIS ABB=ON  PLU=ON  (L36 OR L37 OR L38)


=> d que nos L63
```

```
L5              STR
L7           47 SEA FILE=REGISTRY SSS FUL L5
L24         162 SEA FILE=CAPLUS ABB=ON  PLU=ON  KITAJIMA A?/AU
L25           3 SEA FILE=CAPLUS ABB=ON  PLU=ON  AKIHIKO K?/AU
L26           5 SEA FILE=CAPLUS ABB=ON  PLU=ON  KAMODA O?/AU
L27          22 SEA FILE=CAPLUS ABB=ON  PLU=ON  OSAMU K?/AU
L28           6 SEA FILE=CAPLUS ABB=ON  PLU=ON  OHSAKO A?/AU
L29           2 SEA FILE=CAPLUS ABB=ON  PLU=ON  AKIHIRO O?/AU
L30         574 SEA FILE=CAPLUS ABB=ON  PLU=ON  YANAGI T?/AU
L31           1 SEA FILE=CAPLUS ABB=ON  PLU=ON  TOSHIHARU Y?/AU
L58         252 SEA FILE=BIOSIS ABB=ON  PLU=ON  (L24 OR L25 OR L26 OR L27 OR
                L28 OR L29 OR L30 OR L31)
L60             SEL  PLU=ON  L7 1- CHEM :       49 TERMS
L61           3 SEA FILE=BIOSIS ABB=ON  PLU=ON  L60
L62           5 SEA FILE=BIOSIS ABB=ON  PLU=ON  FAUC65 OR TKS159
L63           2 SEA FILE=BIOSIS ABB=ON  PLU=ON  L58 AND (L61 OR L62)


=> s L59 or L63

L78           5 L59 OR L63

=> file uspatall

FILE 'USPATFULL' ENTERED AT 13:46:07 ON 26 OCT 2006
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FILE 'USPAT2' ENTERED AT 13:46:07 ON 26 OCT 2006
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=> d que nos L73

L24         162 SEA FILE=CAPLUS ABB=ON  PLU=ON  KITAJIMA A?/AU
L25           3 SEA FILE=CAPLUS ABB=ON  PLU=ON  AKIHIKO K?/AU
L26           5 SEA FILE=CAPLUS ABB=ON  PLU=ON  KAMODA O?/AU
L27          22 SEA FILE=CAPLUS ABB=ON  PLU=ON  OSAMU K?/AU
L28           6 SEA FILE=CAPLUS ABB=ON  PLU=ON  OHSAKO A?/AU
L29           2 SEA FILE=CAPLUS ABB=ON  PLU=ON  AKIHIRO O?/AU
L30         574 SEA FILE=CAPLUS ABB=ON  PLU=ON  YANAGI T?/AU
L31           1 SEA FILE=CAPLUS ABB=ON  PLU=ON  TOSHIHARU Y?/AU
L32         165 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L24 OR L25)
L33          27 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L26 OR L27)
L34           8 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L28 OR L29)
L35         575 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L30 OR L31)
L36           1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L32 AND (L33 OR L34 OR L35)
L37           5 SEA FILE=CAPLUS ABB=ON  PLU=ON  L33 AND (L34 OR L35)
L38           1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L34 AND L35
L42           2 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L36 OR L37 OR L38)
L73           7 SEA L42


=> d que nos L74

L5              STR
L7           47 SEA FILE=REGISTRY SSS FUL L5
L11      105205 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?STOMACH?/BI
L12       42051 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?MOTIL?/BI
L13        4188 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?PERISTAL?/BI
L14      249583 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?DIGEST?/BI
L15      288318 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?INTESTIN?/BI
```

```
L16        43191 SEA FILE=CAPLUS ABB=ON  PLU=ON  (5HT OR 5 HT?)/BI
L17        77545 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?SEROTONIN?/BI
L18        22550 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?ILEUM?/BI
L19        18576 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?JEJUN?/BI
L20        31539 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?DUODEN?/BI
L21       139482 SEA FILE=CAPLUS ABB=ON  PLU=ON  TRACT#/BI
L22       171670 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?GASTR?/BI
L24          162 SEA FILE=CAPLUS ABB=ON  PLU=ON  KITAJIMA A?/AU
L25            3 SEA FILE=CAPLUS ABB=ON  PLU=ON  AKIHIKO K?/AU
L26            5 SEA FILE=CAPLUS ABB=ON  PLU=ON  KAMODA O?/AU
L27           22 SEA FILE=CAPLUS ABB=ON  PLU=ON  OSAMU K?/AU
L28            6 SEA FILE=CAPLUS ABB=ON  PLU=ON  OHSAKO A?/AU
L29            2 SEA FILE=CAPLUS ABB=ON  PLU=ON  AKIHIRO O?/AU
L30          574 SEA FILE=CAPLUS ABB=ON  PLU=ON  YANAGI T?/AU
L31            1 SEA FILE=CAPLUS ABB=ON  PLU=ON  TOSHIHARU Y?/AU
L41          235 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L24 OR L25 OR L26 OR L27 OR
                 L28 OR L29 OR L30 OR L31)
L69            4 SEA L7
L70       308291 SEA (L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR
                 L19 OR L20 OR L21 OR L22)
L71            3 SEA L69 AND L70
L72          183 SEA L41
L74            1 SEA L72 AND (L69 OR L71)


=> s L73 or L74

L79            7 L73 OR L74

=> => dup rem L75 L76 L77 L78 L79
FILE 'CAPLUS' ENTERED AT 13:46:50 ON 26 OCT 2006
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FILE 'USPAT2' ENTERED AT 13:46:50 ON 26 OCT 2006
CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)
PROCESSING COMPLETED FOR L75
PROCESSING COMPLETED FOR L76
PROCESSING COMPLETED FOR L77
PROCESSING COMPLETED FOR L78
PROCESSING COMPLETED FOR L79
L80           12 DUP REM L75 L76 L77 L78 L79 (12 DUPLICATES REMOVED)
                 ANSWERS '1-6' FROM FILE CAPLUS
                 ANSWERS '7-9' FROM FILE BIOSIS
                 ANSWERS '10-12' FROM FILE USPATFULL

=> d ibib abs hitind hitstr L80 1-6; d iall L80 7-9; d ibib abs kwic hitstr L80
10-12
```

L80 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2006:953499 CAPLUS
TITLE: In vitro activity of a novel antimicrobial agent, TG44, for treatment of Helicobacter pylori infection
AUTHOR(S): ***Kamoda, Osamu***; Anzai, Kinsei; Mizoguchi, Jun-ichi; Shiojiri, Masatoshi; ***Yanagi, Toshiharu***; Nishino, Takeshi; Kamiya, Shigeru
CORPORATE SOURCE: Quality Assurance Division, Nagase ChemteX Corporation, 1-58-1, Osadano-cho, Fukuchiyama, Kyoto, 620-0853, Japan
SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(9), 3062-3069
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Due to concerns about the current therapeutic modalities for Helicobacter pylori infection, e.g., the increased emergence of drug-resistant strains and the adverse reactions of drugs currently administered, there is a need to develop an anti-H. pylori agent with higher efficacy and less toxicity. The antibacterial activity of TG44, an anti-H. pylori agent with a novel structural formula, against 54 clin. isolates of H. pylori was examined and compared with those of amoxicillin (AMX), clarithromycin (CLR), and metronidazole (MNZ). Consequently, TG44 inhibited the growth of H. pylori in an MIC range of 0.0625 to 1 μg/mL. The MIC ranges of AMX, CLR, and MNZ were 0.0078 to 8 μg/mL, 0.0156 to 64 μg/mL, and 2 to 128 μg/mL, resp. The antibacterial activity of TG44 against AMX-, CLR-, and MNZ-resistant strains was nearly comparable to that against drug-susceptible ones. In a pH range of 3 to 7, TG44 at 3.13 to 12.5 μg/mL exhibited potent bactericidal activity against H. pylori in the stationary phase of growth as early as 1 h after treatment began, in contrast to AMX, which showed no bactericidal activity at concns. of up to 50 μg/mL at the same time point of treatment. TG44 at 25 μg/mL exhibited no antibacterial activity against 13 strains of aerobic bacteria, suggesting that its antibacterial activity against H. pylori is potent and highly specific. The present study indicated that TG44 possesses antibacterial activity which manifests quickly and is potentially useful for eradicating not only the antibiotic-susceptible but also the antibiotic-resistant strains of H. pylori by monotherapy.
CC 10-5 (Microbial, Algal, and Fungal Biochemistry)
IT INDEXING IN PROGRESS
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2000:172222 CAPLUS
DOCUMENT NUMBER: 132:301171
TITLE: Preparation and characterization of two crystalline forms of 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]benzamide (TKS159)
AUTHOR(S): ***Yanagi, Toshiharu***; Mizoguchi, Jun-Ichi; Adachi, Tsutomu; Sato, Seiji; Kodama, Kazuya; Anzai, Kinsei; Takagishi, Yasushi; Kamei, Chiaki; Fujiwara, Manabu; Matsushita, Takayuki; Yamashoji, Yuko; Inoue, Yoshihisa
CORPORATE SOURCE: Research and Development Department, Teikoku Chemical Industries Co., Ltd., Hyogo, 664-0898, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (2000), 48(3), 366-369

CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB For 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]benzamide (TKS159), two polymorphs, forms α and β, were prepared and characterized by x-ray powder diffractometry, thermal anal., IR spectroscopy and 13C-NMR spectroscopy, both in the solution and solid phases. The x-ray powder diffraction anal. gave different patterns for forms α and β. In the TG and DTA profiles, form β exhibited characteristic endo- and exothermic peaks at 112.7° and 116.2°, resp., due to the partial melting-induced phase transition to form α without accompanying weight loss, and these were followed by an addnl. endothermic peak at 138.2° due to fusion. For form α, only an endothermic peak at 137.8° due to fusion was observed The IR spectroscopic analyses of forms α and β gave different absorption bands assigned to N-H and O-H stretching, N-H bending, and C=O stretching vibrations. From the data obtained by thermal anal., form α is thermodynamically more stable than form β.

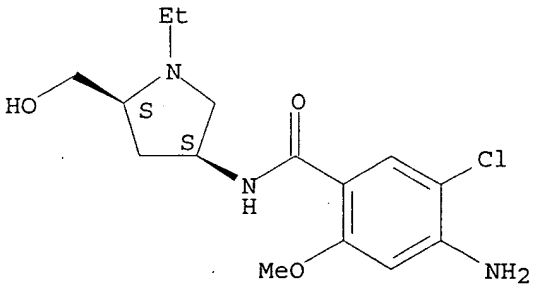
CC 75-7 (Crystallography and Liquid Crystals)
Section cross-reference(s): 27

IT ***142228-17-9P***, TKS159
RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(preparation and characterization of crystalline forms of)

IT ***142228-17-9P***, TKS159
RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(preparation and characterization of crystalline forms of)

RN 142228-17-9 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 1999:765890 CAPLUS
DOCUMENT NUMBER: 132:122464
TITLE: Synthesis and pharmacological activity of 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]benzamide (TKS159) and its optical isomers
AUTHOR(S): ***Yanagi, Toshiharu***; Katajima, Akihiko; Anzai, Kinsei; Kodama, Kazuya; Mizoguchi, Jun-Ichi; Fujiwara, Hiromichi; Sakiyama, Hideyo; ***Kamoda, Osamu***;

Kamei, Chiaki
CORPORATE SOURCE: Research and Development Department, Teikoku Chemical Industries Co., Ltd., Hyogo, 664-0898, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1999), 47(11), 1650-1654
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB TKS159 and its optical isomers were prepared from optically active 4-amino-1-ethyl-2-hydroxymethylpyrrolidine di-p-toluenesulfonates, which were prepared from a com. available trans-4-hydroxy-L-proline. The absolute configurations of TKS159 and its isomers were spectroscopically determined All the isomers showed a relatively potent affinity for 5-hydroxytryptamine 4 (***5-HT4***) receptors in a radioligand binding assay ([3H]GR113808). The other isomers were less effective than TKS159 for the ***gastric*** emptying of a phenol red semisolid meal in rats. All this suggests that the most potent of the isomers was 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]benzamide (TKS159).

CC 27-10 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST hydroxymethylpyrrolidinylbenzamide TKS159 isomer prepn ***serotoninergic***; ***gastric*** emptying hydroxymethylpyrrolidinylbenzamide TKS159 isomer

IT ***5-HT*** agonists
(***5-HT4***; preparation and pharmacol. activity of TKS159 and its optical isomers)

IT ***Gastric*** emptying
(preparation and pharmacol. activity of TKS159 and its optical isomers)

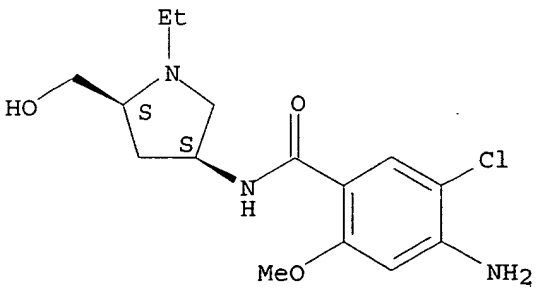
IT ***142228-17-9P***, TKS159 ***142228-19-1P 142228-20-4P 142228-21-5P***
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and pharmacol. activity of TKS159 and its optical isomers)

IT ***142228-17-9P***, TKS159 ***142228-19-1P 142228-20-4P 142228-21-5P***
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and pharmacol. activity of TKS159 and its optical isomers)

RN 142228-17-9 CAPLUS

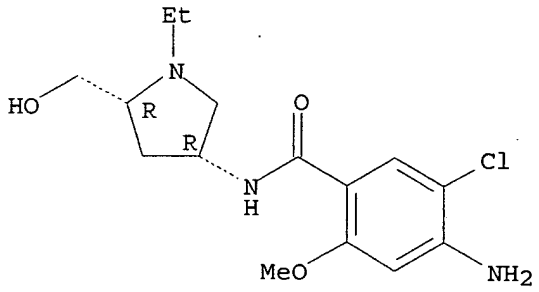
CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



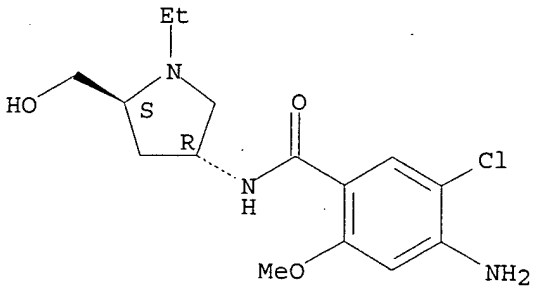
RN 142228-19-1 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[(3R,5R)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



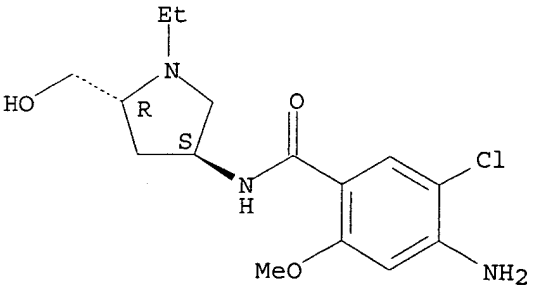
RN 142228-20-4 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[(3R,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 142228-21-5 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[(3S,5R)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:252338 CAPLUS
DOCUMENT NUMBER: 140:264507

TITLE: Medicinal composition for improving ***digestive tract*** movement

INVENTOR(S): ***Kitajima, Akihiko; Kamoda, Osamu; Ohsako, Akihiro; Yanagi, Toshiharu***

PATENT ASSIGNEE(S): Nagase Chemtex Corporation, Japan

SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004024143	A1	20040325	WO 2002-JP9390	20020912
W: AE, AG, AL, AM, AU, AZ, BA, BB, BR, BY, BZ, CA, CN, CO, CR, CU, DM, DZ, EC, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, RU, SG, SI, TJ, TM, TN, TT, UA, US, UZ, VC, VN, YU, ZA				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002335161	A1	20040430	AU 2002-335161	20020912
EP 1547593	A1	20050629	EP 2002-807809	20020912
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CN 1668295	A	20050914	CN 2002-829602	20020912
US 2005239861	A1	20051027	US 2005-526780	20050520

PRIORITY APPLN. INFO.: WO 2002-JP9390 A 20020912

AB An ameliorant for improving the movement of the ***digestive tract*** which is rich in binding affinity for a ***serotonin*** receptor 4 (5HT4), causes no disorders such as arteritis and thrombus formation, and contains as an active ingredient 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof, which is a product of metabolism of 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof; a medicinal composition for improving the movement of the ***digestive tract*** which comprises the ameliorant and a pharmaceutically acceptable support, is rich in binding affinity for a ***serotonin*** receptor 4 (5HT4), and causes no disorders such as arteritis and thrombus formation; and a treatment for enhancing the movement of the ***digestive tract*** which comprises using the medicinal composition

IC ICM A61K031-40
ICS A61P001-14; C07D207-08

CC 1-9 (Pharmacology)
Section cross-reference(s): 63

ST ***hypoperistalsis digestive tract*** movement ***serotonin*** receptor arteritis thrombus

IT ***5-HT*** agonists
(***5-HT4***; medicinal composition for improving ***digestive tract*** movement)

IT Dopamine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D2; medicinal composition for improving ***digestive tract*** movement)

IT Artery, disease
Inflammation
(arteritis; medicinal composition for improving ***digestive***

tract movement)

IT ***Digestive tract***, disease
(***hypoperistalsis***; medicinal composition for improving ***digestive tract*** movement)

IT Thrombus
(medicinal composition for improving ***digestive tract*** movement)

IT Drug delivery systems
(tablets; medicinal composition for improving ***digestive tract*** movement)

IT ***5-HT*** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type ***5-HT4***; medicinal composition for improving ***digestive tract*** movement)

IT ***672285-79-9P***
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(medicinal composition for improving ***digestive tract*** movement)

IT 24201-13-6, 4-Acetylamino-5-chloro-2-methoxy-benzoic acid 33996-30-4, 4-Hydroxy-L-proline-ethyl ester hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(medicinal composition for improving ***digestive tract*** movement)

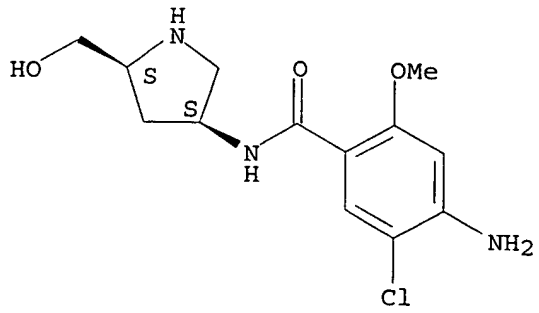
IT 33996-28-0P 672285-80-2P 672285-81-3P 672285-82-4P 672285-83-5P ***672285-84-6P***
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(medicinal composition for improving ***digestive tract*** movement)

IT ***672285-79-9P***
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(medicinal composition for improving ***digestive tract*** movement)

RN 672285-79-9 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)

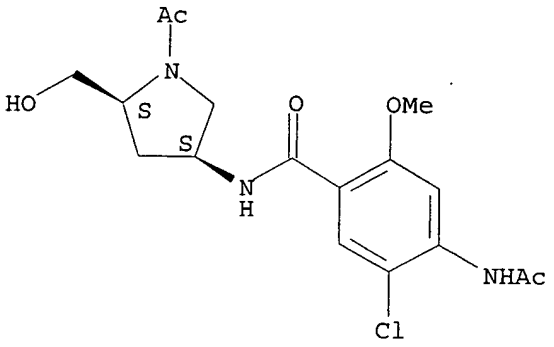
Absolute stereochemistry.



● HCl

IT *672285-84-6P*
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(medicinal composition for improving ***digestive tract*** movement)
RN 672285-84-6 CAPLUS
CN Benzamide, 4-(acetylamino)-N-[(3S,5S)-1-acetyl-5-(hydroxymethyl)-3-pyrrolidinyl]-5-chloro-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:503261 CAPLUS
DOCUMENT NUMBER: 127:113344
TITLE: Trans-4-guanidinomethylcyclohexanecarboxylic acid esters for inhibition of Helicobacter pylori
INVENTOR(S): ***Kamoda, Osamu***; ***Yanagi, Toshiharu***; Tamaki, Eiji; Sato, Seiji; Mizoguchi, Jun-ichi
PATENT ASSIGNEE(S): Teikoku Chemical Industries Co., Ltd., Japan
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9723207	A1	19970703	WO 1996-JP3723	19961220
W: AU, CN, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9711716	A1	19970717	AU 1997-11716	19961220
EP 870500	A1	19981014	EP 1996-942589	19961220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 3468244	B2	20031117	JP 1997-523501	19961220
TW 457086	B	20011001	TW 1996-85115861	19970120
TW 225786	B1	20050101	TW 2001-90111426	19970120
US 6444703	B1	20020903	US 1998-91588	19980812
US 2002123508	A1	20020905		
AU 763893	B2	20030731	AU 2001-19709	20010212
PRIORITY APPLN. INFO.:			JP 1995-354660 A	19951222
			WO 1996-JP3723 W	19961220

AB A drug composition which comprises a combination of 4-[4-(4-methylbenzyloxycarbonyl)phenyl]phenyl trans-4-guanidinomethylcyclohexanecarboxylate (I) or an acid addition salt thereof and a cyclodextrin, especially β-cyclodextrin, is suitable for removing or exterminating Helicobacter pylori. I·HCl 4 g was dissolved in 120 mL aqueous solution containing 8.46 g β-cyclodextrin and freeze-dried. The product showed an improved solubility

IC ICM A61K031-24
ICS A61K047-40

CC 63-5 (Pharmaceuticals)

L80 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:431362 CAPLUS
DOCUMENT NUMBER: 125:86328
TITLE: Preparation of guanidinomethylcyclohexanecarboxylic acid aryl ester derivatives as antibacterial agents against Helicobacter pylori infection
INVENTOR(S): ***Kamoda, Osamu***; Fujiwara, Hiromichi; ***Yanagi, Toshiharu***
PATENT ASSIGNEE(S): Teikoku Chemical Industries Co., Ltd., Japan
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9606825	A1	19960307	WO 1995-JP1725	19950830
W: JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 775692	A1	19970528	EP 1995-930012	19950830
EP 775692	B1	20001206		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
EP 989112	A2	20000329	EP 1999-124756	19950830
EP 989112	A3	20001115		
EP 989112	B1	20040414		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
AT 197950	E	20001215	AT 1995-930012	19950830
ES 2153902	T3	20010316	ES 1995-930012	19950830
PT 775692	T	20010531	PT 1995-930012	19950830

crystals, concentrated in vacuo, treated with dry pyridine, ice-cooled, treated with 1.50 g trans-4-guanidinomethylcyclohexanecarboxylic acid hydrochloride, and stirred overnight under water-cooling to give 2.44 g trans-I.HCl (Ar = Q). The latter compound showed min. inhibitory concentration of
0.20, 0.39, and >25 μg/mL against Helicobacter pylori ATCC 43504 and ATCC 43629 and Escherichia coli NIH JC-2, resp. Each dispersant, capsule, and suspension formulation containing I (Ar = Q1) was prepared

IC ICM C07C279-14
ICS A61K031-215; A61K031-275

CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1

L80 ANSWER 7 OF 12 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 3

ACCESSION NUMBER: 2002:545501 BIOSIS
DOCUMENT NUMBER: PREV200200545501
TITLE: Cyclohexane carbocyclic ester derivative and cyclodextrin complex and composition for treatment of helicobacter pylori infections.
AUTHOR(S): ***Kamoda, Osamu*** [Inventor, Reprint author]; ***Yanagi, Toshiharu*** [Inventor]; Tamaki, Eiji [Inventor]; Sato, Seiji [Inventor]; Mizoguchi, Jun-ichi [Inventor]
CORPORATE SOURCE: Hyogo, Japan
ASSIGNEE: Teikoku Chemical Industries Co., Ltd., Osaka, Japan
PATENT INFORMATION: US 6444703 20020903
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Sep. 3, 2002) Vol. 1262, No. 1. http://www.uspto.gov/web/menu/patdata.html. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Oct 2002
Last Updated on STN: 23 Oct 2002

ABSTRACT:The present invention relates to a pharmaceutical composition which is appropriate for eradication or extermination of Helicobacter pylori wherein [4-[4-(4-methylbenzyloxycarbonyl)phenyl[phenyl trans-4-guanidinomethylcyclohexanecarboxylate or an acid addition salt thereof are compounded and it also relates to a complex consisting them.

NAT. PATENT. CLASSIF.:514553000
CONCEPT CODE: Pharmacology - General 22002
Physiology and biochemistry of bacteria 31000
Chemotherapy - General, methods and metabolism 38502
Chemotherapy - Antibacterial agents 38504
INDEX TERMS: Major Concepts
Pharmacology
INDEX TERMS: Diseases
Helicobacter pylori infection: bacterial disease
Helicobacter Infections (MeSH)
INDEX TERMS: Chemicals & Biochemicals
[4-[4-(4-methylbenzyloxycarbonyl)phenyl[phenyl trans-4-guanidinomethylcyclohexanecarboxylate: antibacterial-drug, antiinfective-drug; cyclodextrin complex: antibacterial-drug, antiinfective-drug; cyclohexane carbocyclic ester derivative:

antibacterial-drug, antiinfective-drug

ORGANISM: Classifier
Aerobic Helical or Vibrioid Gram-Negatives 06210
Super Taxa
Eubacteria; Bacteria; Microorganisms
Organism Name
Helicobacter pylori: pathogen
Taxa Notes
Bacteria, Eubacteria, Microorganisms

L80 ANSWER 8 OF 12 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 4
ACCESSION NUMBER: 2001:521744 BIOSIS
DOCUMENT NUMBER: PREV200100521744
TITLE: Guanidinomethyl cyclohexane carboxylic acid ester derivatives.
AUTHOR(S): ***Kamoda, Osamu*** [Inventor, Reprint author]; Fujiwara, Hiromichi [Inventor]; ***Yanagi, Toshiharu*** [Inventor]
CORPORATE SOURCE: Itami, Japan
ASSIGNEE: Teikoku Chemical Industries Co., Ltd., Osaka, Japan
PATENT INFORMATION: US 6284791 20010904
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Sep. 4, 2001) Vol. 1250, No. 1. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Nov 2001
Last Updated on STN: 23 Feb 2002

ABSTRACT:A compound represented by general formula (I-2) or a pharmaceutically acceptable acid-addition salt thereof, useful as an anti-microbial against Helicobacter pylori and as a medicinal composition for treating Helicobacter pylori infection, wherein Ar represents phenyl, biphenyl or naphthyl each having a at least one substituent selected from the group consisting of halogen, cyano, nitro, carboxy, C1 -C18 alkyl, C1 -C18 alkoxy, C3 -C18 cycloalkyl, C7 -C18 aralkyl, C8 -C18 arylalkenyl, C7 -C18 aralkyloxy, optionally substituted phenoxy, optionally substituted C2 -C19 alkoxycarbonyl, and optionally substituted C8 -C19 aralkyloxycarbonyl, provided the case where Ar represents phenyl substituted by halogen, cyano, nitro, carboxy, C1 -C18 alkyl, optionally substituted C2 -C19 alkoxycarbonyl or C8 -C19 aralkyloxycarbonyl is expected.

NAT. PATENT. CLASSIF.:514529000
CONCEPT CODE: General biology - Miscellaneous 00532
INDEX TERMS: Major Concepts
Methods and Techniques; Pharmacology
INDEX TERMS: Diseases
Helicobacter pylori infection: bacterial disease, treatment
Helicobacter Infections (MeSH)
INDEX TERMS: Chemicals & Biochemicals
guanidinomethyl cyclohexane carboxylic acid ester derivatives: antibacterial-drug
ORGANISM: Classifier
Aerobic Helical or Vibrioid Gram-Negatives 06210
Super Taxa
Eubacteria; Bacteria; Microorganisms
Organism Name
Helicobacter pylori
Taxa Notes

APPLICATION INFO.: US 2003-623135 A1 20030718 (10)
RELATED APPLN. INFO.: Division of Ser. No. US 2000-721182, filed on 22 Nov 2000, GRANTED, Pat. No. US 6831190 Division of Ser. No. US 1997-793728, filed on 28 Feb 1997, GRANTED, Pat. No. US 6284791

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1994-243489	19940830
	JP 1994-243490	19940830
	JP 1994-248270	19940905
	JP 1994-252655	19940909
	WO 1995-JP1725	19950830

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: EDWARDS & ANGELL, LLP, P.O. BOX 55874, BOSTON, MA, 02205
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: CLM-01-14
LINE COUNT: 2064
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to novel and valuable intermediate compounds of the general formula (VIII) which can be used for the preparation of novel compounds comprising an antibacterial action, especially with a strong antibacterial action against helicobacter pylori, and pharmaceutically acceptable salts thereof. In the general formula (VIII) X is hydrogen or halogen, Y is hydrogen or a substituted or unsubstituted aralkyloxycarbonyl group having 8-19 carbon atoms, Z is hydrogen, a substituted aralkyloxycarbonyl group having 8-19 carbon atoms or a substituted alkoxycarbonyyl group having 2-19 carbon atoms, except that X, Y and Z are all hydrogen. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN ***Kamoda, Osamu***, Itami-shi, JAPAN
IN ***Yanagi, Toshiharu***, Itami-shi, JAPAN

L80 ANSWER 11 OF 12 USPATFULL on STN
ACCESSION NUMBER: 2005:275296 USPATFULL
TITLE: Medicinal composition
INVENTOR(S): ***Kitajima, Akihiko***, Fukuchiyama-shi, JAPAN
Kamoda, Osamu, Fukuchiyama-shi, JAPAN
Ohsako, Akihiro, Fukuchiyama-shi, JAPAN
Yanagi, Toshiharu, Osaka-shi, JAPAN

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005239861	A1	20051027	
APPLICATION INFO.:	US 2003-526780	A1	20020912	(10)
	WO 2002-JP9390		20020912	
			20050520	PCT 371 date

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: WENDEROTH, LIND & PONACK, L.L.P., 2033 K STREET N. W., SUITE 800, WASHINGTON, DC, 20006-1021, US
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Page(s)
LINE COUNT: 859
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to an ameliorant for improving the

movement of the ***digestive tract*** comprising, as an active ingredient, 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pirrolidinyl]benzamide or an acid addition salt thereof which is a metabolite of 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof, having high biding affinity for a ***serotonin*** receptor 4 (***5HT***.sub.4) and causing no arteritis and thrombus formation; a medicinal composition for improving the movement of the ***digestive tract*** comprising the said ameliorant and a pharmaceutically acceptable carrier; and a treating method for promoting the movement of the ***digestive tract***, which comprises using the said medicinal composition for improving the movement of the ***digestive tract***.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IN ***Kitajima, Akihiko***, Fukuchiyama-shi, JAPAN

IN ***Kamoda, Osamu***, Fukuchiyama-shi, JAPAN

IN ***Ohsako, Akihiro***, Fukuchiyama-shi, JAPAN

IN ***Yanagi, Toshiharu***, Osaka-shi, JAPAN

AB The present invention relates to an ameliorant for improving the movement of the ***digestive tract*** comprising, as an active ingredient, 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pirrolidinyl]benzamide or an acid addition salt thereof which is a metabolite of 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof, having high biding affinity for a ***serotonin*** receptor 4 (***5HT***.sub.4) and causing no arteritis and thrombus formation; a medicinal composition for improving the movement of the ***digestive tract*** comprising the said ameliorant and a pharmaceutically acceptable carrier; and a treating method for promoting the movement of the ***digestive tract***, which comprises using the said medicinal composition for improving the movement of the ***digestive tract***.

SUMM The present invention relates to an ameliorant for improving the movement of the ***digestive tract*** of a human and an animal containing as an active ingredient a compound which is suitable for activating the movement of the ***digestive tract***, inter alia, ***stomach*** to rapidly eliminate abnormal retention of an ingested food in the organ, has a peripheral acting site, and has no. . . . comprising the active ingredient and a pharmaceutically acceptable carrier, a method for improving disorder of the movement dysfunction of the ***digestive tract*** comprising administering a composition containing an effective amount of the active compound to a patient, and use of the compound. . .

SUMM . . . compound having a generic name of metoclopramide is widely known as a compound having nature of promoting the movement of ***stomach***, but induces extrapyramidal disorder and other undesirable disorders due to action on central nervous system. In addition, a compound having a generic name of cisapride has been put into practice as a ***digestive tract*** movement activator, but use thereof has been stopped due to inducement of ventricular arrhythmia.

SUMM . . . extremely weak action on central nervous system is known as a compound having action of promoting the movement of the ***digestive tract***, inter alia, ***stomach*** (JP-A-17434/1993). However, the present applicant progressed development of TKS159 which is a representative compound of the invention of the above. . . that 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof is a compound having the ability of improving the movement of the ***digestive***

tract equivalent to or superior over that of TKS159 or an acid addition salt thereof. That is, it was found out. . . . thrombus formation, arteritis, encephalomalacia and the like can be effectively used as an ameliorant for improving the movement of the ***digestive tract*** containing this compound as an active ingredient. Needless to say, it is natural that desired attribute of a drug used. . . .

SUMM . . . . invention has been made based on the aforementioned findings, and relates to an ameliorant for improving the movement of the ***digestive tract***, which avoids side effect such as arteritis, containing 4-amino-5-chloro-2-methoxy-N-[(2S, 4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof as an active ingredient. . . .

SUMM The ameliorant for improving the movement of the ***digestive tract*** of the present invention and a novel medicinal composition containing the same relate to a novel medicinal composition comprising a. . . .

SUMM . . . . salt is superior over TKS159 or an acid addition salt thereof in the ability to improve the movement of the ***digestive tract***. Further, it was also made clear that 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof acts as an agonist such that binding with a ***serotonin*** 4 (***5HT***.sub.4) receptor is preferential to binding to other receptor, for example, a dopamine D.sub.2 receptor.

SUMM . . . . various new findings and, according to the present invention, there are provided an ameliorant for improving the movement of the ***digestive tract*** containing as an active ingredient 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof, which has high binding affinity for a ***serotonin*** receptor 4 (***5HT***.sub.4), and can avoid occurrence of side effect such as thrombus formation, arteritis and the like inevitably caused concomitantly in administration. . . .

SUMM . . . . serious side effect is confirmed. That is, the present invention relates to an ameliorant for improving the movement of the ***digestive tract*** which has been confirmed to bean effective and safe medicine not accompanied with occurrence of side effect.

SUMM (1) an ameliorant for improving the movement of the ***digestive tract*** comprising as an active ingredient 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof, which has high binding affinity for a ***serotonin*** receptor 4 (***5HT***.sub.4), and does not cause arteritis and thrombus formation,

SUMM (2) a medicinal composition for improving the movement of the ***digestive tract***, comprising as an active ingredient 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof, which has high binding affinity for a ***serotonin*** receptor 4 (***5HT***.sub.4), and does not cause arteritis and thrombus formation, and a pharmaceutically acceptable carrier,

SUMM (3) a treating method for promoting the movement of the ***digestive tract***, which comprises using an ameliorant for improving the movement of the ***digestive tract*** comprising as an active ingredient 4-amino-5-chloro-2-methoxy-N-[(2S, 4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof, which is has high binding affinity for a ***serotonin*** receptor 4 (***5HT***.sub.4), and does not cause arteritis and thrombus formation, or using a medicinal composition for improving the movement of the ***digestive tract*** comprising the

ameliorant and a pharmaceutically acceptable carrier,

SUMM (4) a method for improving the movement of the ***digestive tract*** of a human or an animal, while avoiding occurrence of arteritis, thrombus formation or encephalomalacia, which comprises administering 4-amino-5-chloro-2-methoxy-N-[(2S, 4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide. . .

DRWD FIG. 1 shows a change in binding affinity for a ***serotonin*** receptor 4, of a specimen drug. An abscissa axis indicates a concentration (molar concentration; logarithmic expression) of a specimen drug, and an ordinate axis indicates a ratio of binding of a ***serotonin*** receptor 4 and [.sup.3H] GR113808. .largecircle. - - - .largecircle. indicates a specimen compound obtained in Example 9, and .circle-solid.. . . .circle-solid. indicates TKS159 hydrochloride. As a concentration of a specimen drug grows higher, an amount of [.sup.3H]GR113808 bound to a ***serotonin*** receptor 4 is reduced. That is, it is indicated that a specimen drug binds to a ***serotonin*** receptor 4, antagonizing [.sup.3H]GR113808 binding to the ***serotonin*** receptor 4. It is seen that affinity of a specimen drug obtained in Example 9 for a ***serotonin*** receptor 4 is stronger as compared with affinity of TKS159 hydrochloride.

DETD . . . compound of the formula (III) can be used like TM161, since it exerts effect of improving the movement of the ***digestive tract*** more excellent than that of TKS159 while avoiding side effect such as thrombus formation, arteritis and encephalomalacia. Examples of a. . .

DETD 4-Amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide of the present invention or an acid addition salt thereof, which has high binding affinity for a ***serotonin*** receptor 4 (***5HT***.sub.4) and does not cause arteritis, thrombus formation and the like is a metabolite of 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt. . .

DETD Thus, an ameliorant for improving the movement of the ***digestive tract*** which has high binding affinity for a ***serotonin*** receptor 4 (***5HT***.sub.4) and can avoid side effect occurred concomitantly in TKS159 or an acid addition salt thereof such as arteritis and thrombus. . .

DETD 4-Amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof obtained herein, which is an ameliorant for improving the movement of the ***digestive tract*** having high binding affinity for a ***serotonin*** receptor 4 (***5HT***.sub.4) and being capable of avoiding side effect that concomitantly occurs in association with TKS159 or an acid addition salt thereof,. . . a pharmaceutically acceptable suitable carrier, and is put into practice as a medicinal composition for improving the movement of the ***digestive tract***.

DETD As the preparation of a formulated medicinal composition of the present invention for improving the movement of the ***digestive tract*** comprising 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof which is an ameliorant for improving the movement of the ***digestive tract***, having high binding affinity for a ***serotonin*** receptor 4 (***5HT***.sub.4) and being capable of avoiding side effect that concomitantly occurs in association with TKS159 or an acid addition salt thereof. . . the aforementioned carriers. For example, when a preparation which is a formulated medicinal composition for improving the movement of the ***digestive tract*** is a tablet, a prescribed amount of 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-

pyrrolidinyl]benzamide or an acid addition salt thereof, which is an ameliorant for improving the movement of the ***digestive tract***, having high binding affinity for a ***serotonin*** receptor 4 (***5HT***.sub.4) and being capable of avoiding side effect that concomitantly occurs in association with TKS159 or an acid addition salt thereof. . .

DETD . . . content of 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof which is an ameliorant for improving of the movement of the ***tract*** having high binding affinity for a ***serotonin*** receptor 4 (***5HT***.sub.4) and being capable of avoiding side effect that concomitantly occurs in association with TKS159 or an acid addition salt thereof. . .

DETD 4-Amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrollidinyl]benzamide or an acid addition salt thereof which is an ameliorant for improving the movement of the ***digestive tract*** having high binding affinity for a ***serotonin*** receptor 4 (***5HT***.sub.4) and being capable of avoiding side effect that concomitantly occurs in association with TKS159 or an acid addition salt thereof,. . . toxicity test, and is therefore suitable in oral administration. There are provided an ameliorant for improving the movement of the ***digestive tract*** comprising, as an active ingredient, 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pirrolidinyl]benzamide or an acid addition salt thereof which is a metabolite of 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof, having high biding affinity for a ***serotonin*** receptor 4 (***5HT***.sub.4) and causing no arteritis and thrombus formation, and a medicinal composition for improving the movement of the ***digestive tract*** comprising the same and a carrier.

DETD Measurement of Action of 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide monohydrochloride on ***serotonin*** receptor 4

DETD . . . pig was homogenized in a 50 mM HEPES-NaOH buffer (pH 7.4), and centrifugation and suspension were repeated to prepare a ***serotonin*** receptor 4 sample. The receptor sample was reacted with a solution containing a 0.1 nM radioactive ligand of [.sup.3H]-GR113808 and. . . of the filter was measured using a scintillation counter (LS6500 Beckman), so that affinity of the specimen drug for a ***serotonin*** receptor 4 was measured. Separately, the same procedure was also performed regarding TKS159 hydrochloride, and the affinity was compared.

DETD . . . specimen was forcibly administered orally at 9 o'clock to 12 o'clock for 28 days once a day using a rat ***stomach*** tube. Only a 0.5% aqueous methylcellulose solution was administered at 10 ml/kg to a control group.

DETD Regarding the drug obtained in Example 9, a degree of action of promoting the movement of the ***digestive tract*** was measured using an esophagus sample extracted from a rat.

DETD . . . one case, necrosis of an artery septum and surrounding cell infiltration were recognized in cerebellumpiamater, lung, coronary artery, liver, bladder, ***stomach***, vagina, ***intestine*** and diaphragm. Separately, beagle dogs (female and male) were divided into 4 groups containing 5, 3, 3 and 5 dogs. . .

DETD In the present invention, an ameliorant for improving the movement of the ***digestive tract*** comprising, as an active ingredient, 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof which has high binding affinity for a ***serotonin*** receptor 4 (***5HT*** .sub.4) and capable of avoiding side effect occurrence such as thrombus

formation and arteritis concomitantly caused inevitably in administration of 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]benzamide. . .

CLM What is claimed is:

1. An ameliorant for improving the movement of the ***digestive tract***, comprising as an active ingredient 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof which has high binding affinity for a ***serotonin*** receptor 4 (***5HT***.sub.4) and does not cause arteritis and thrombus formation.

2. A medicinal composition for improving the movement of the ***digestive tract***, comprising as an active ingredient 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof which has high binding affinity for a ***serotonin*** receptor 4 (***5HT*** .sub.4) and does not cause arteritis and thrombus formation, and a pharmaceutically acceptable carrier.

3. A treating method for promoting the movement of the ***digestive tract***, which comprises using an ameliorant for improving the movement of the ***digestive tract*** comprising as an active ingredient 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or an acid addition salt thereof which has high binding affinity for a ***serotonin*** receptor 4 (***5HT*** .sub.4) and does not cause arteritis and thrombus formation, or using a medicinal composition for improving the movement of the ***digestive tract*** comprising the ameliorant and a pharmaceutically acceptable carrier.

4. A method for improving the movement of the ***digestive tract*** of a human or an animal while avoiding occurrence of arteritis, thrombus formation or encephalomalacia, which comprises administering 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-2-hydroxymethyl-4-pyrrolidinyl]benzamide or. . .

IT ***672285-79-9P***
(medicinal composition for improving digestive tract movement)

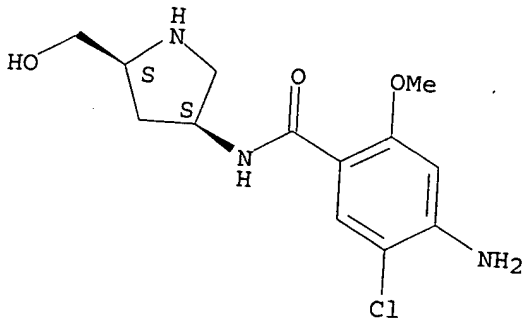
IT 33996-28-0P 672285-80-2P 672285-81-3P 672285-82-4P 672285-83-5P ***672285-84-6P***
(medicinal composition for improving digestive tract movement)

IT ***672285-79-9P***
(medicinal composition for improving digestive tract movement)

RN 672285-79-9 USPATFULL

CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)

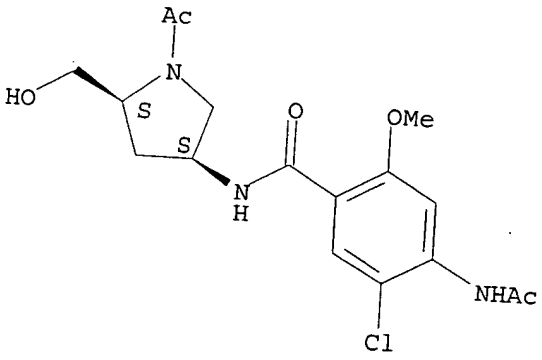
Absolute stereochemistry.



● HCl

IT *672285-84-6P*
(medicinal composition for improving digestive tract movement)
RN 672285-84-6 USPATFULL
CN Benzamide, 4-(acetylamino)-N-[(3S,5S)-1-acetyl-5-(hydroxymethyl)-3-pyrrolidinyl]-5-chloro-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L80 ANSWER 12 OF 12 USPATFULL on STN
ACCESSION NUMBER: 2004:317320 USPATFULL
TITLE: Guanidinomethyl cyclohexane carboxylic acid ester derivatives
INVENTOR(S): ***Kamoda, Osamu***, Itami, JAPAN
Fujiwara, Hiromichi, Itami, JAPAN
Yanagi, Toshiharu, Itami, JAPAN
PATENT ASSIGNEE(S): Teikoku Chemical Industries Co., Ltd., Osaka, JAPAN (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6831190	B1	20041214
APPLICATION INFO.:	US 2000-721182		20001122 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1997-793728, filed on 28 Feb 1997		

	NUMBER	DATE

Searched by John DiNatale x2-2557

PRIORITY INFORMATION: JP 1994-243489 19940830
JP 1994-243490 19940830
JP 1994-248270 19940905
JP 1994-252655 19940909
DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Barts, Samuel
LEGAL REPRESENTATIVE: Corless, Peter F., Alexander, John B., Edwards & Angell, LLP
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 2000
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to novel and valuable intermediate compounds of the general formula (VIII) which can be used for the preparation of novel compounds comprising an antibacterial action, especially with a strong antibacterial action against helicobacter pylori, and pharmaceutically acceptable salts thereof. In the general formula (VIII) X is hydrogen or halogen, Y is hydrogen or a substituted or unsubstituted aralkyloxycarbonyl group having 8-19 carbon atoms, Z is hydrogen, a substituted aralkyloxycarbonyl group having 8-19 carbon atoms or a substituted alkoxycarbonyyl group having 2-19 carbon atoms, except that X, Y and Z are all hydrogen. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IN ***Kamoda, Osamu***, Itami, JAPAN
IN ***Yanagi, Toshiharu***, Itami, JAPAN

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L5                STR
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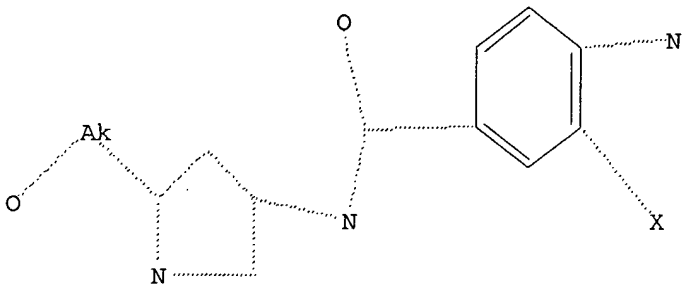


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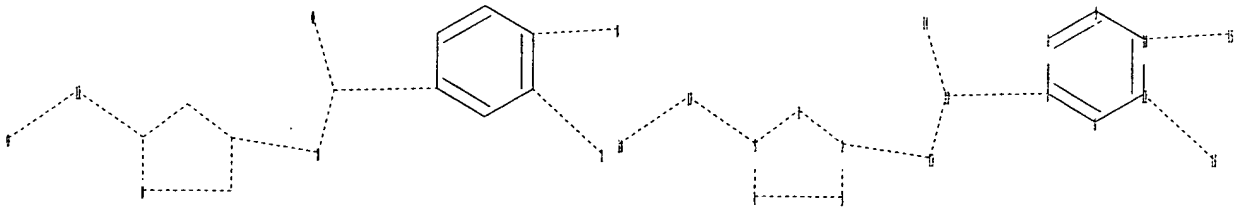

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=> d que nos L23

L5              STR
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L18       22550 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?ILEUM?/BI
L19       18576 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?JEJUN?/BI
L20       31539 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?DUODEN?/BI
L21      139482 SEA FILE=CAPLUS ABB=ON  PLU=ON  TRACT#/BI
L22      171670 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?GASTR?/BI
L23          12 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND (L11 OR L12 OR L13 OR
                L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22)


=> s (L8 or L23) not L75

L81          15 (L8 OR L23) NOT L75

=> file medline

FILE 'MEDLINE' ENTERED AT 13:51:10 ON 26 OCT 2006

 FILE LAST UPDATED: 25 Oct 2006 (20061025/UP).  FILE COVERS 1950 TO DATE.

 On December 11, 2005, the 2006 MeSH terms were loaded.

 The MEDLINE reload for 2006 is now (26 Feb.) available.  For details
 on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
 See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

 OLDMEDLINE is covered back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2006 vocabulary.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que nos L44

L5              STR
L7           47 SEA FILE=REGISTRY SSS FUL L5
L43             SEL  PLU=ON  L7 1- CHEM :      49 TERMS
L44           3 SEA FILE=MEDLINE ABB=ON  PLU=ON  L43


=> d que nos L46

L46           5 SEA FILE=MEDLINE ABB=ON  PLU=ON  TKS159
```

```
=> d que nos L48

L5              STR
L7           47 SEA FILE=REGISTRY SSS FUL L5
L11      105205 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?STOMACH?/BI
L12       42051 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?MOTIL?/BI
L13        4188 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?PERISTAL?/BI
L14      249583 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?DIGEST?/BI
L15      288318 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?INTESTIN?/BI
L16       43191 SEA FILE=CAPLUS ABB=ON  PLU=ON  (5HT OR 5 HT?)/BI
L17       77545 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?SEROTONIN?/BI
L18       22550 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?ILEUM?/BI
L19       18576 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?JEJUN?/BI
L20       31539 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?DUODEN?/BI
L21      139482 SEA FILE=CAPLUS ABB=ON  PLU=ON  TRACT#/BI
L22      171670 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?GASTR?/BI
L43             SEL  PLU=ON  L7 1- CHEM :      49 TERMS
L44           3 SEA FILE=MEDLINE ABB=ON  PLU=ON  L43
L45           0 SEA FILE=MEDLINE ABB=ON  PLU=ON  FAUC65
L46           5 SEA FILE=MEDLINE ABB=ON  PLU=ON  TKS159
L47     1149902 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L11 OR L12 OR L13 OR L14 OR
                L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22)
L48           5 SEA FILE=MEDLINE ABB=ON  PLU=ON  L47 AND ((L44 OR L45 OR L46))


=> s (L44 or L46 or L48) not L76

L82           3 (L44 OR L46 OR L48) NOT L76

=> file embase

FILE 'EMBASE' ENTERED AT 13:51:14 ON 26 OCT 2006
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 FILE COVERS 1974 TO 26 Oct 2006 (20061026/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 EMBASE is now updated daily.  SDI frequency remains weekly (default)
 and biweekly.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que nos L53

L5              STR
L7           47 SEA FILE=REGISTRY SSS FUL L5
L52             SEL  PLU=ON  L7 1- CHEM :      49 TERMS
L53           7 SEA FILE=EMBASE ABB=ON  PLU=ON  L52


=> d que nos L54

L54           4 SEA FILE=EMBASE ABB=ON  PLU=ON  FAUC65 OR TKS159


=> d que nos L56
```

```
L5              STR
L7           47 SEA FILE=REGISTRY SSS FUL L5
L11      105205 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?STOMACH?/BI
L12       42051 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?MOTIL?/BI
L13        4188 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?PERISTAL?/BI
L14      249583 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?DIGEST?/BI
L15      288318 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?INTESTIN?/BI
L16       43191 SEA FILE=CAPLUS ABB=ON  PLU=ON  (5HT OR 5 HT?)/BI
L17       77545 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?SEROTONIN?/BI
L18       22550 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?ILEUM?/BI
L19       18576 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?JEJUN?/BI
L20       31539 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?DUODEN?/BI
L21      139482 SEA FILE=CAPLUS ABB=ON  PLU=ON  TRACT#/BI
L22      171670 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?GASTR?/BI
L52             SEL  PLU=ON  L7 1- CHEM :      49 TERMS
L53           7 SEA FILE=EMBASE ABB=ON  PLU=ON  L52
L54           4 SEA FILE=EMBASE ABB=ON  PLU=ON  FAUC65 OR TKS159
L56           7 SEA FILE=EMBASE ABB=ON  PLU=ON  (L53 OR L54) AND (L11 OR L12
                OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21
                OR L22)


=> s (L53 or L54 or L56) not L77

L83           5 (L53 OR L54 OR L56) NOT L77

=> file biosis

FILE 'BIOSIS' ENTERED AT 13:51:18 ON 26 OCT 2006
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 18 October 2006 (20061018/ED)


=> d que nos L61

L5              STR
L7           47 SEA FILE=REGISTRY SSS FUL L5
L60             SEL  PLU=ON  L7 1- CHEM :      49 TERMS
L61           3 SEA FILE=BIOSIS ABB=ON  PLU=ON  L60


=> d que nos L62

L62           5 SEA FILE=BIOSIS ABB=ON  PLU=ON  FAUC65 OR TKS159


=> s L61-L62 not L78

L84           3 (L61 OR L62) NOT L78

=> file uspatall

FILE 'USPATFULL' ENTERED AT 13:51:21 ON 26 OCT 2006
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FILE 'USPAT2' ENTERED AT 13:51:21 ON 26 OCT 2006
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=> d que nos L69

L5              STR
L7             47 SEA FILE=REGISTRY SSS FUL L5
L69             4 SEA L7


=> d que nos L71

L5              STR
L7             47 SEA FILE=REGISTRY SSS FUL L5
L11        105205 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?STOMACH?/BI
L12         42051 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?MOTIL?/BI
L13          4188 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?PERISTAL?/BI
L14        249583 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?DIGEST?/BI
L15        288318 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?INTESTIN?/BI
L16         43191 SEA FILE=CAPLUS ABB=ON  PLU=ON  (5HT OR 5 HT?)/BI
L17         77545 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?SEROTONIN?/BI
L18         22550 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?ILEUM?/BI
L19         18576 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?JEJUN?/BI
L20         31539 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?DUODEN?/BI
L21        139482 SEA FILE=CAPLUS ABB=ON  PLU=ON  TRACT#/BI
L22        171670 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?GASTR?/BI
L69             4 SEA L7
L70        308291 SEA (L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR
                  L19 OR L20 OR L21 OR L22)
L71             3 SEA L69 AND L70


=> s (L69 or L71) not L79

L85             3 (L69 OR L71) NOT L79

=> dup rem L81 L82 L83 L84 L85
FILE 'CAPLUS' ENTERED AT 13:53:56 ON 26 OCT 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE 'MEDLINE' ENTERED AT 13:53:56 ON 26 OCT 2006

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FILE 'BIOSIS' ENTERED AT 13:53:56 ON 26 OCT 2006
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FILE 'USPATFULL' ENTERED AT 13:53:56 ON 26 OCT 2006
CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)
PROCESSING COMPLETED FOR L81
PROCESSING COMPLETED FOR L82
PROCESSING COMPLETED FOR L83
PROCESSING COMPLETED FOR L84
PROCESSING COMPLETED FOR L85
L86            22 DUP REM L81 L82 L83 L84 L85 (7 DUPLICATES REMOVED)
                  ANSWERS '1-15' FROM FILE CAPLUS
                  ANSWER '16' FROM FILE MEDLINE
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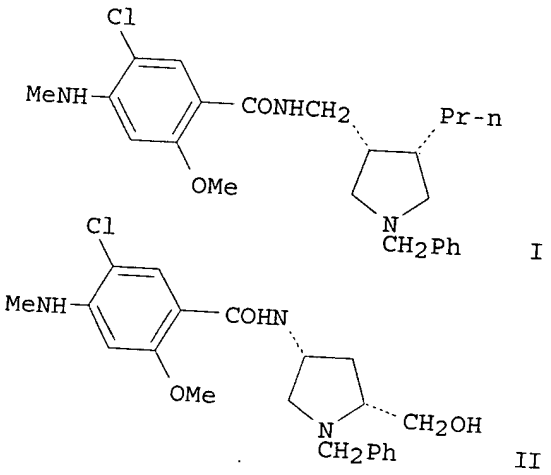
ANSWERS '17-18' FROM FILE EMBASE
ANSWER '19' FROM FILE BIOSIS
ANSWERS '20-22' FROM FILE USPATFULL

=> d ibib abs hitind hitstr L86 1-15; d iall L86 16-19; d ibib abs kwic hitstr L86 20-22

L86 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2003:804055 CAPLUS
DOCUMENT NUMBER: 140:5276
TITLE: Ex-chiral pool synthesis and receptor binding studies of 4-substituted prolinol derivatives
AUTHOR(S): Heindl, Cornelia; Hubner, Harald; Gmeiner, Peter
CORPORATE SOURCE: Emil Fischer Center, Department of Medicinal Chemistry, Friedrich Alexander University, Erlangen, D-91052, Germany
SOURCE: Tetrahedron: Asymmetry (2003), 14(20), 3141-3152
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:5276
GI



I

II

AB Starting from natural 4-hydroxyproline, preparation of the four possible stereoisomers of 4-amino- and 4-aminomethyl-substituted prolinol derivs., resp., was accomplished by chemo- and regioselective functional group transformations at the 2- and 4-positions of the pyrrolidine moiety. These building blocks were used as valuable precursors for the preparation of new methoxybenzamide derivs. Dopamine and ***serotonin*** binding studies involving the subtypes D1, D2long, D2short, D3 and D4 as well as ***5-HT1A*** and ***5-HT2***, resp., displayed interesting structure activity relationships, especially with respect to the absolute and relative configuration of the test compds. As a complement to the D3 receptor-preferring aminomethylpyrrolidine FAUC 21 (I; prepared by the authors in an earlier work), one of the title compds., (2R,4R)-aminoprolinol derivative II (FAUC 65), was found to preferentially recognize D4 subtype.

CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 2, 27

Searched by John DiNatale x2-2557

ST prolinol methoxybenzamide deriv prepn dopamine ***serotonin*** receptor binding; aminomethylprolinol aminoprolinol deriv prepn hydroxyproline precursor

IT Dopamine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D1; preparation of methoxybenzamide derivs. of amino/aminomethyl-substituted prolinols and their binding of dopamine and ***serotonin*** receptors)

IT Dopamine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D1A; preparation of methoxybenzamide derivs. of amino/aminomethyl-substituted prolinols and their binding of dopamine and ***serotonin*** receptors)

IT Dopamine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D2(long); preparation of methoxybenzamide derivs. of amino/aminomethyl-substituted prolinols and their binding of dopamine and ***serotonin*** receptors)

IT Dopamine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D2(short); preparation of methoxybenzamide derivs. of amino/aminomethyl-substituted prolinols and their binding of dopamine and ***serotonin*** receptors)

IT Dopamine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D3; preparation of methoxybenzamide derivs. of amino/aminomethyl-substituted prolinols and their binding of dopamine and ***serotonin*** receptors)

IT Dopamine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D4; preparation of methoxybenzamide derivs. of amino/aminomethyl-substituted prolinols and their binding of dopamine and ***serotonin*** receptors)

IT Structure-activity relationship
(dopaminergic receptor-binding; preparation of methoxybenzamide derivs. of amino/aminomethyl-substituted prolinols and their binding of dopamine and ***serotonin*** receptors)

IT Structure-activity relationship
(***serotoninergic*** receptor-binding; preparation of methoxybenzamide derivs. of amino/aminomethyl-substituted prolinols and their binding of dopamine and ***serotonin*** receptors)

IT ***5-HT*** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type ***5-HT1A***; preparation of methoxybenzamide derivs. of amino/aminomethyl-substituted prolinols and their binding of dopamine and ***serotonin*** receptors)

IT ***5-HT*** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type ***5-HT2***; preparation of methoxybenzamide derivs. of amino/aminomethyl-substituted prolinols and their binding of dopamine and ***serotonin*** receptors)

IT 15676-16-1, Sulpiride 229322-99-0, FAUC 21
RL: PAC (Pharmacological activity); BIOL (Biological study)
(comparisons of dopamine and ***serotonin*** receptor-binding activities)

IT ***627100-88-3P*** ***627100-89-4P*** 627100-90-7P 627100-91-8P ***627100-93-0P*** 627100-95-2P ***627100-97-4P*** ***627101-23-9P*** 627101-24-0P 627101-25-1P ***627529-76-4P***, FAUC 65
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL

(Biological study); PREP (Preparation)
(preparation of methoxybenzamide derivs. of amino/aminomethyl-substituted prolinols and their binding of dopamine and ***serotonin*** receptors)

IT 51-35-4 24201-13-6 61478-25-9 61694-98-2 107746-25-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of methoxybenzamide derivs. of amino/aminomethyl-substituted prolinols and their binding of dopamine and ***serotonin*** receptors)

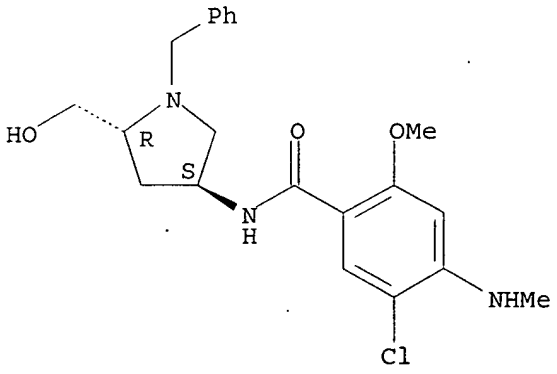
IT 77449-94-6P 77449-99-1P 114677-02-0P 142292-37-3P 154342-88-8P
154343-00-7P 171192-72-6P 627100-71-4P 627100-72-5P 627100-73-6P
627100-74-7P 627100-75-8P 627100-76-9P 627100-77-0P 627100-78-1P
627100-79-2P 627100-80-5P 627100-81-6P 627100-82-7P 627100-83-8P
627100-84-9P 627100-85-0P 627100-86-1P 627100-99-6P 627101-01-3P
627101-07-9P 627101-10-4P 627101-12-6P 627101-14-8P 627101-16-0P
627101-18-2P 627101-20-6P 627101-22-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of methoxybenzamide derivs. of amino/aminomethyl-substituted prolinols and their binding of dopamine and ***serotonin*** receptors)

IT 627100-87-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of methoxybenzamide derivs. of amino/aminomethyl-substituted prolinols and their binding of dopamine and ***serotonin*** receptors)

IT ***627100-88-3P 627100-89-4P 627100-93-0P 627100-97-4P 627101-23-9P 627529-76-4P***, FAUC 65
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of methoxybenzamide derivs. of amino/aminomethyl-substituted prolinols and their binding of dopamine and ***serotonin*** receptors)

RN 627100-88-3 CAPLUS
CN Benzamide, 5-chloro-N-[(3S,5R)-5-(hydroxymethyl)-1-(phenylmethyl)-3-pyrrolidinyl]-2-methoxy-4-(methylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

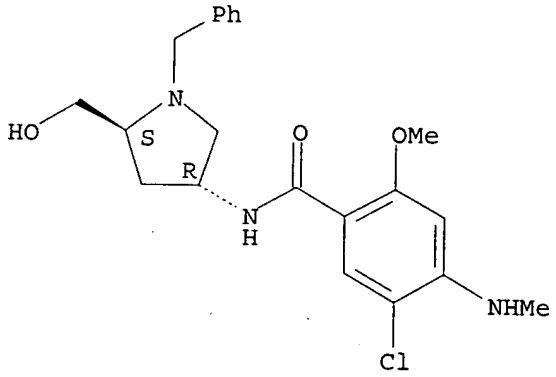


RN 627100-89-4 CAPLUS
CN Benzamide, 5-chloro-N-[(3S,5S)-5-(hydroxymethyl)-1-(phenylmethyl)-3-pyrrolidinyl]-2-methoxy-4-(methylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

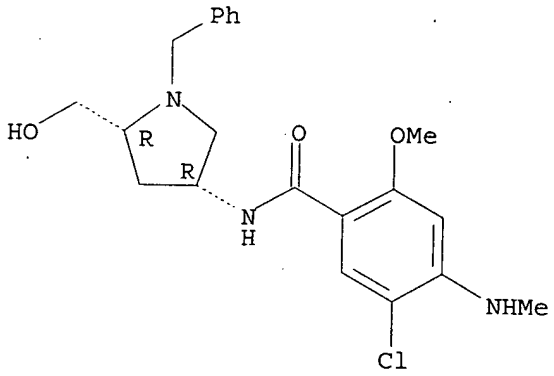
pyrrolidinyl]-2-methoxy-4-(methylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 627529-76-4 CAPLUS
CN Benzamide, 5-chloro-N-[(3R,5R)-5-(hydroxymethyl)-1-(phenylmethyl)-3-pyrrolidinyl]-2-methoxy-4-(methylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L86 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 1998:679340 CAPLUS
DOCUMENT NUMBER: 130:47331
TITLE: Effects of ***gastrointestinal*** prokinetic agents, TKS159 and cisapride, on the in situ canine heart assessed by cardiohemodynamic and electrophysiological monitoring
AUTHOR(S): Sugiyama, Atsushi; Hashimoto, Keitaro
CORPORATE SOURCE: Department of Pharmacology, Yamanashi Medical University, Yamanashi, 409-3898, Japan
SOURCE: Toxicology and Applied Pharmacology (1998), 152(1), 261-269
CODEN: TXAPA9; ISSN: 0041-008X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Effects of a novel ***5-HT4*** receptor agonist TKS159 on

the cardiovascular system were assessed in comparison with cisapride using an in vivo canine model. TKS159 in doses of 0.1, 1.0, and 10 mg/kg (n = 6) or cisapride in 1/10 doses of 0.01, 0.1, and 1.0 mg/kg (n = 6) was cumulatively infused over 10 min with a pause of 20 min. The doses of the drugs were determined according to the previous knowledge of their pharmacokinetics. Clin. effective plasma concns. as a ***gastrointestinal*** prokinetic drug were obtained after the infusion of 0.1 mg/kg of the resp. drugs. In TKS159-administered animals, no significant change was induced in each cardiovascular parameter by an infusion of 0.1 mg/kg. The blood pressure was decreased, and the effective refractory period and repolarization phase of the ventricle were prolonged after 1.0 mg/kg. The heart rate was decreased, and the atrioventricular, as well as intraventricular, conduction were suppressed after 10 mg/kg, while no significant changes were observed in the cardiac output and the ventricular contraction and the relative refractory period of the ventricle during the study. Meanwhile, in cisapride-administered animals, the repolarization phase and the effective refractory period were prolonged after 0.01 mg/kg. The heart rate and the blood pressure were decreased after 0.1 mg/kg. The cardiac output, the ventricular contraction, and the atrioventricular conduction were suppressed, the relative refractory period was prolonged, and early after-depolarization was detected after 1.0 mg/kg, while no significant change was observed in the intraventricular conduction during the study. Thus, TKS159 may have a safer cardiovascular profile than cisapride. (c) 1998 Academic Press.

CC 1-9 (Pharmacology)

IT ***5-HT*** receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(***5-HT4***; effects of ***gastrointestinal*** prokinetic agent, TKS159, on cardiovascular system in comparison with cisapride)

IT Toxicity
(cardiotoxicity; effects of ***gastrointestinal*** prokinetic agent, TKS159, on cardiovascular system in comparison with cisapride)

IT Toxicity
(drug; effects of ***gastrointestinal*** prokinetic agent, TKS159, on cardiovascular system in comparison with cisapride)

IT Blood pressure
Cardiovascular system
Heart rate
(effects of ***gastrointestinal*** prokinetic agent, TKS159, on cardiovascular system in comparison with cisapride)

IT Heart
(toxicity; effects of ***gastrointestinal*** prokinetic agent, TKS159, on cardiovascular system in comparison with cisapride)

IT Cardiac contraction
(ventricular; effects of ***gastrointestinal*** prokinetic agent, TKS159, on cardiovascular system in comparison with cisapride)

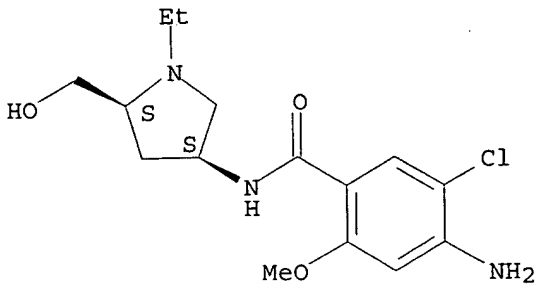
IT 81098-60-4, Cisapride ***142228-17-9***, TKS159
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(effects of ***gastrointestinal*** prokinetic agent, TKS159, on cardiovascular system in comparison with cisapride)

IT ***142228-17-9***, TKS159
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(effects of ***gastrointestinal*** prokinetic agent, TKS159, on cardiovascular system in comparison with cisapride)

RN 142228-17-9 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L86 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1996:170355 CAPLUS
DOCUMENT NUMBER: 124:221382
TITLE: Identification of putative 5-hydroxytryptamine4 (***5-HT4***) receptors in guinea pig ***stomach***: the effect of TKS159, a novel agonist, on ***gastric motility*** and acetylcholine release
AUTHOR(S): Matsuyama, Shogo; Sakiyama, Hideyo; Nei, Koji; Tanaka, Chikako
CORPORATE SOURCE: Sch. Med., Kobe Univ., Kobe, 650, Japan
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1996), 276(3), 989-95
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors investigated the existence and the function of 5-hydroxytryptamine4 (***5-HT4***) receptors and the effect of TKS159, a novel agonist of ***5-HT4*** receptor, on guinea pig ***stomach***. The mech. activity and the release of [3H]ACh were measured using prepns. of muscle layers attached to intramural plexus from guinea pig ***stomach***. ***5-HT*** in the presence of 1 μM methysergide, 1 μM ketanserin and 1 μM granisetron, 5-methoxytryptamine or TKS159 enhanced the elec. transmural stimulation-evoked contraction and [3H]ACh release in strips of the ***stomach*** in a concentration-dependent manner. This enhancement by ***5-HT***, 5-methoxytryptamine or TKS159 was antagonized by SDZ 205-557 or atropine. Cisapride, metoclopramide and TKS159 enhanced the elec. transmural stimulation-evoked contraction and release of [3H]ACh in a concentration-dependent manner. The authors conclude that the pharmacol. characteristics of the receptor, which mediates contraction of the guinea pig ***stomach*** by the activation of cholinergic nerves, are consistent with its being of the putative ***5-HT4*** receptor type and that TKS159 is an agonist at ***5-HT4*** receptors.

CC 2-8 (Mammalian Hormones)
Section cross-reference(s): 1

ST ***serotonin*** S4 receptor ***stomach*** acetylcholine; TKS 159 ***stomach motility*** acetylcholine

IT ***Stomach***
(***serotonin*** S4 receptor characterization in guinea pig ***stomach*** and TKS 159 effect on ***gastric***

motility and acetylcholine release)

IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(***serotoninergic*** S4, ***serotonin*** S4 receptor characterization in guinea pig ***stomach*** and TKS 159 effect on ***gastric motility*** and acetylcholine release)

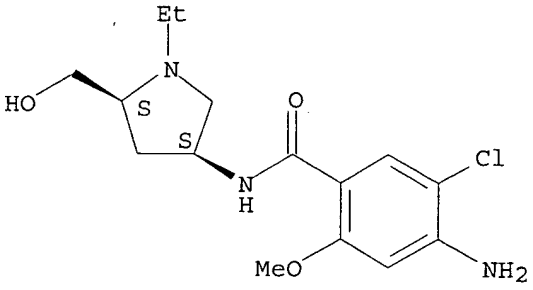
IT 50-67-9, ***Serotonin***, biological studies 608-07-1, 5-Methoxytryptamine ***142228-17-9***, TKS 159
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(***serotonin*** S4 receptor characterization in guinea pig ***stomach*** and TKS 159 effect on ***gastric motility*** and acetylcholine release)

IT 51-84-3, Acetylcholine, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(***serotonin*** S4 receptor characterization in guinea pig ***stomach*** and TKS 159 effect on ***gastric motility*** and acetylcholine release)

IT ***142228-17-9***, TKS 159
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(***serotonin*** S4 receptor characterization in guinea pig ***stomach*** and TKS 159 effect on ***gastric motility*** and acetylcholine release)

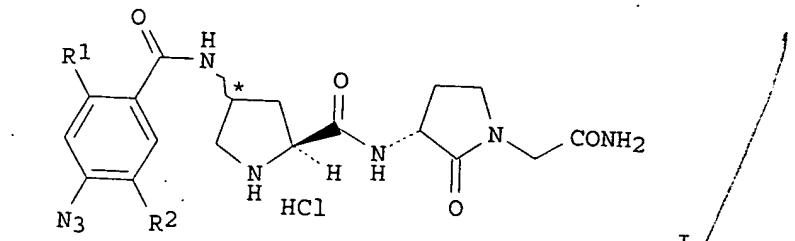
RN 142228-17-9 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L86 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1255208 CAPLUS
DOCUMENT NUMBER: 144:150625
TITLE: Design and Synthesis of Photoaffinity-Labeling Ligands of the L-Prolyl-L-leucylglycinamide Binding Site Involved in the Allosteric Modulation of the Dopamine Receptor
AUTHOR(S): Fisher, Abigail; Mann, Amandeep; Verma, Vaneeta; Thomas, Nancy; Mishra, Ram K.; Johnson, Rodney L.
CORPORATE SOURCE: Department of Medicinal Chemistry, University of Minnesota, Minneapolis, MN, 55455-0343, USA
SOURCE: Journal of Medicinal Chemistry (2006), 49(1), 307-317
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal

LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:150625
GI



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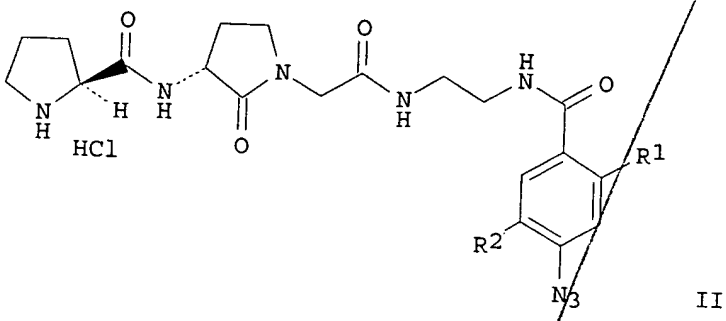


II

AB Peptide H-Pro-Leu-Gly-NH2 (PLG), in addition to its endocrine effects, possesses the ability to modulate dopamine D2 receptors within the central nervous system. However, the precise binding site of PLG is unknown. Potential photoaffinity-labeling ligands of the PLG binding site were designed as tools to be used in the identification of the macromol. that possesses this binding site. Photoaffinity-labeling ligands, PLG peptidomimetics I (both trans and cis diastereomers at *'d locant were obtained) and II, were designed and synthesized. The 4-azidobenzoyl and 4-azido-2-hydroxybenzoyl photoaffinity-labeling moieties were placed at opposite ends of PLG peptidomimetic to generate a series of ligands that potentially could be used to map the PLG binding site. All of the compds. that were synthesized possessed activity comparable to or better than PLG in enhancing [3H]-N-propylnorapomorphine agonist binding to dopamine receptors. Photoaffinity ligands that were cross-linked to the receptor preparation produced a modulatory effect that was either comparable to or greater than the increase in agonist binding produced by the resp. ligands that were not cross-linked to the dopamine receptor. The results indicate that these photoaffinity-labeling agents are binding at the same allosteric site as PLG and PLG peptidomimetics.

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

IT 874163-12-9P 874163-13-0P ***874163-14-1P*** 874163-15-2P
874163-16-3P 874163-23-2P 874163-24-3P 874163-25-4P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of photoaffinity-labeled peptidomimetics of prolylleucylglycinamide to study its binding site involved in allosteric modulation of dopamine receptor)

IT 96602-46-9P 99298-06-3P 185304-19-2P 865295-35-8P 874162-95-5P
874162-96-6P 874162-97-7P 874162-98-8P 874162-99-9P 874163-00-5P
874163-02-7P 874163-03-8P 874163-04-9P 874163-05-0P 874163-06-1P
874163-07-2P ***874163-08-3P*** 874163-09-4P 874163-10-7P

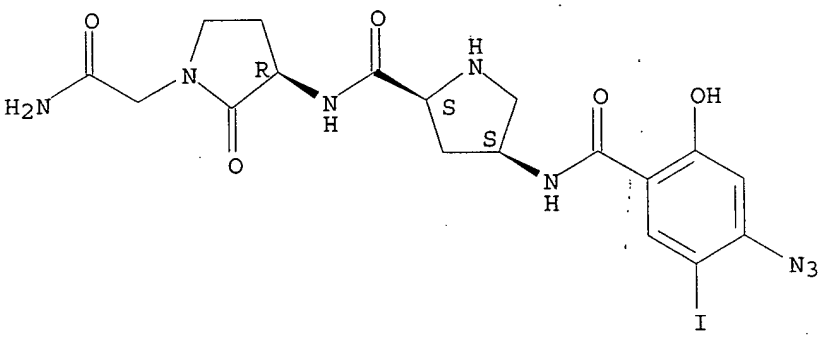
874163-11-8P 874163-18-5P 874163-19-6P 874163-20-9P
874163-21-0P 874163-22-1P 874163-26-5P 877262-55-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and biol. activity of photoaffinity-labeled peptidomimetics of prolylleucylglycinamide to study its binding site involved in allosteric modulation of dopamine receptor)

IT ***874163-17-4P***
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and biol. activity of photoaffinity-labeled peptidomimetics of prolylleucylglycinamide to study its binding site involved in allosteric modulation of dopamine receptor)

IT ***874163-14-1P***
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of photoaffinity-labeled peptidomimetics of prolylleucylglycinamide to study its binding site involved in allosteric modulation of dopamine receptor)

RN 874163-14-1 CAPLUS
CN 1-Pyrrolidineacetamide, 3-[[[(2S,4S)-4-[(4-azido-2-hydroxy-5-iodobenzoyl)amino]-2-pyrrolidinyl]carbonyl]amino]-2-oxo-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

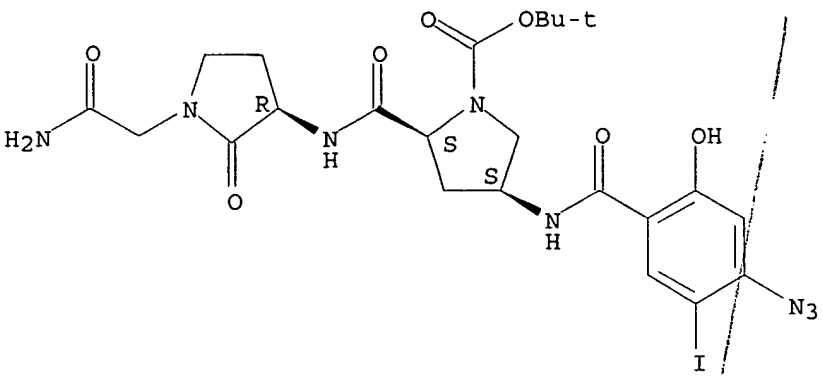


● HCl

IT ***874163-08-3P 874163-11-8P***
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and biol. activity of photoaffinity-labeled peptidomimetics of prolylleucylglycinamide to study its binding site involved in allosteric modulation of dopamine receptor)

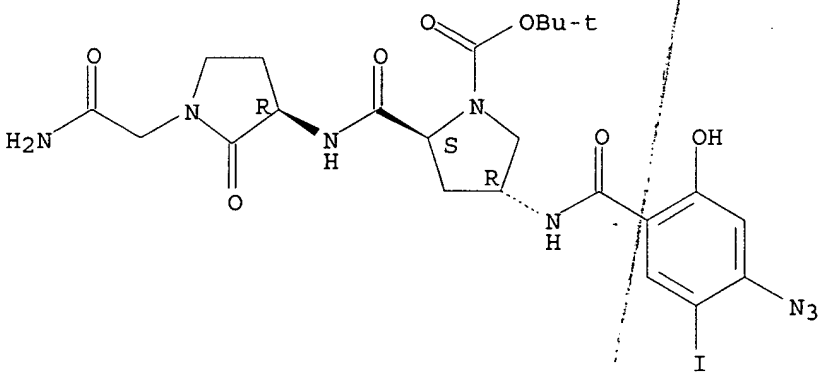
RN 874163-08-3 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 2-[[[(3R)-1-(2-amino-2-oxoethyl)-2-oxo-3-pyrrolidinyl]amino]carbonyl]-4-[(4-azido-2-hydroxy-5-iodobenzoyl)amino]-, 1,1-dimethylethyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



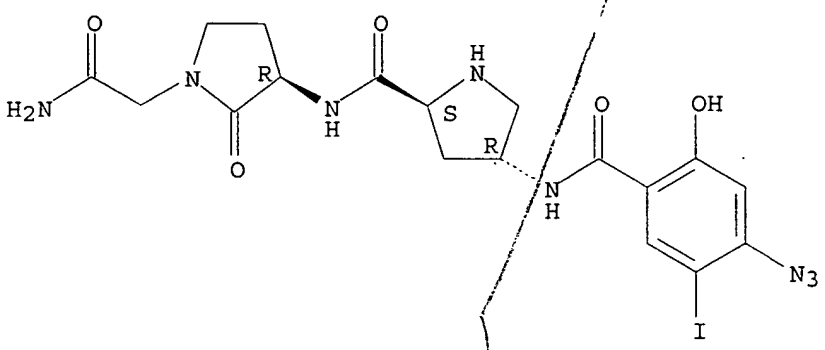
RN 874163-11-8 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 2-[[[(3R)-1-(2-amino-2-oxoethyl)-2-oxo-3-pyrrolidinyl]amino]carbonyl]-4-[(4-azido-2-hydroxy-5-iodobenzoyl)amino]-, 1,1-dimethylethyl ester, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT ***874163-17-4P***
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and biol. activity of photoaffinity-labeled peptidomimetics of prolylleucylglycinamide to study its binding site involved in allosteric modulation of dopamine receptor)
RN 874163-17-4 CAPLUS
CN 1-Pyrrolidineacetamide, 3-[[[(2S,4R)-4-[(4-azido-2-hydroxy-5-iodobenzoyl)amino]-2-pyrrolidinyl]carbonyl]amino]-2-oxo-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

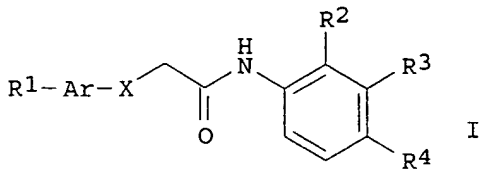
L86 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1311545 CAPLUS
DOCUMENT NUMBER: 144:51586
TITLE: Preparation of acetamide derivatives as reverse transcriptase inhibitors for treatment of HIV
INVENTOR(S): Deroy, Patrick; Faucher, Anne-Marie; Gagnon, Alexandre; Landry, Serge; Morin, Sebastien; O'Meara, Jeffrey; Simoneau, Bruno; Thavonekham, Bounkham; Yoakim, Christiane
PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany; Boehringer Ingelheim Pharma Gmbh & Co KG
SOURCE: PCT Int. Appl., 206 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005118575	A1	20051215	WO 2005-CA907	20050530
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005282907	A1	20051222	US 2005-137831	20050524
CA 2555633	AA	20051215	CA 2005-2555633	20050530

PRIORITY APPLN. INFO.: US 2004-575888P P 20040601
WO 2005-CA907 W 20050530

OTHER SOURCE(S): MARPAT 144:51586

GI



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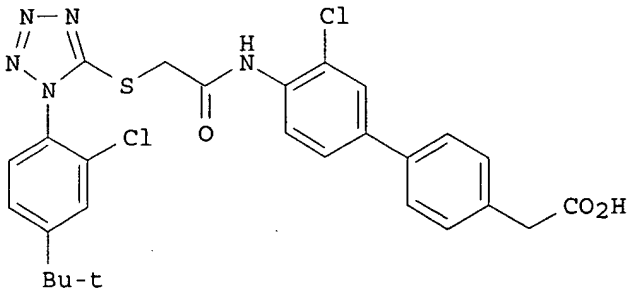

II

AB The title compds. I [wherein Ar = (un)substituted 5-membered aromatic heterocycle; X = O or S; R1 = (un)substituted Ph; R2 = halo, NO2, or alkyl; R3 = H or halo; R4 = (un)substituted Ph, alkenyl, heteroaryl, etc.] or enantiomers, diastereomers, tautomers, or pharmaceutically acceptable salts thereof were prepared as reverse transcriptase inhibitors against wild type and single or double mutant strains of HIV for the treatment or prophylaxis of HIV infection. For example, the compound II was prepared in a multi-step synthesis. The enzymic assay was conducted.

IC ICM C07D403-12
ICS A61K031-41; A61K031-4439; A61K031-454; A61K031-4709; A61K031-495; A61K031-5377; A61K031-541; A61P031-18; C07D257-04; C07D249-04; C07D249-10; C07D277-36; C07D285-06

CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT 871473-75-5P 871473-76-6P 871473-77-7P 871473-78-8P 871473-79-9P
871473-80-2P 871473-81-3P 871473-82-4P 871473-83-5P 871473-84-6P
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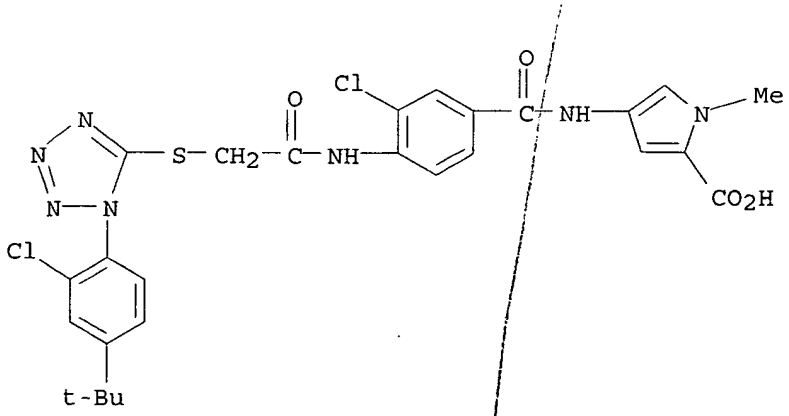
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of acetamide derivs. as reverse transcriptase inhibitors for treatment of HIV infection)

IT ***871475-96-6P***

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of acetamide derivs. as reverse transcriptase inhibitors for treatment of HIV infection)

RN 871475-96-6 CAPLUS

CN 1H-Pyrrole-2-carboxylic acid, 4-[[3-chloro-4-[[[[1-[2-chloro-4-(1,1-dimethylethyl)phenyl]-1H-tetrazol-5-yl]thio]acetyl]amino]benzoyl]amino]-1-methyl- (9CI) (CA INDEX NAME)



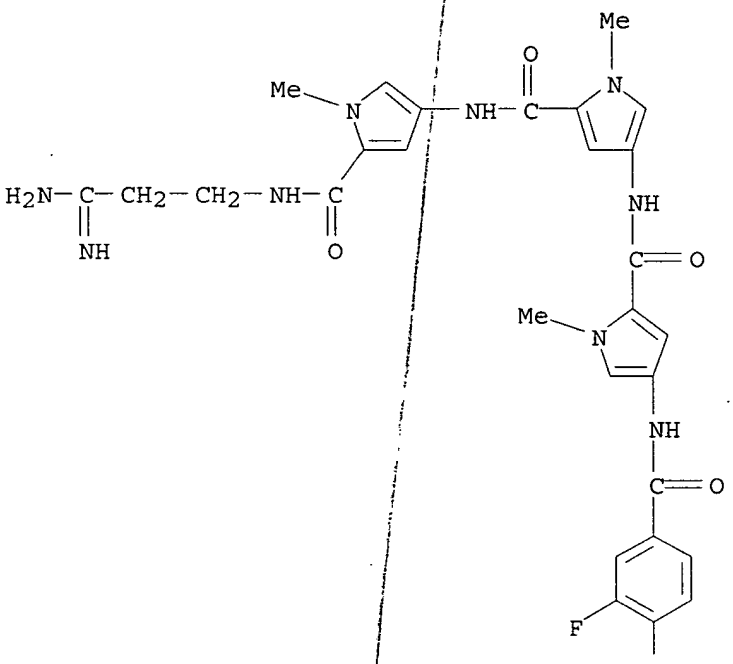
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L86 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

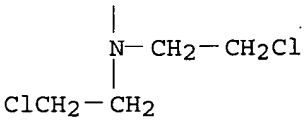
ACCESSION NUMBER: 2004:813105 CAPLUS
DOCUMENT NUMBER: 142:221
TITLE: Hybridized particle swarm algorithm for adaptive structure training of multilayer feed-forward neural network: QSAR studies of bioactivity of organic compounds
AUTHOR(S): Shen, Qi; Jiang, Jian-Hui; Jiao, Chen-Xu; Lin, Wei-Qi; Shen, Guo-Li; Yu, Ru-Qin
CORPORATE SOURCE: State Key Laboratory of Chemo/Biosensing and Chemometrics, College of Chemistry and Chemical Engineering, Hunan University, Changsha, 410082, Peop. Rep. China
SOURCE: Journal of Computational Chemistry (2004), 25(14), 1726-1735
CODEN: JCCHDD; ISSN: 0192-8651
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The multilayer feed-forward ANN is an important modeling technique used in QSAR studying. The training of ANN is usually carried out only to optimize the wts. of the neural network and without paying attention to the network topol. Some other strategies used to train ANN are, first, to discover an optimum structure of the network, and then to find wts. for an already defined structure. These methods tend to converge to local optima, and may also lead to overfitting. In this article, a hybridized particle swarm optimization (PSO) approach was applied to the neural network structure training (HPSONN). The continuous version of PSO was used for the weight training of ANN, and the modified discrete PSO was applied to find appropriate the network architecture. The network structure and connectivity are trained simultaneously. The two versions of PSO can jointly search the global optimal ANN architecture and wts. A new objective function is formulated to determine the appropriate network architecture and optimum value of the wts. The proposed HPSONN algorithm was used to predict carcinogenic potency of aromatic amines and biol. activity of a series of distamycin and distamycin-like derivs. The results were compared to those obtained by PSO and GA training in which the network architecture was kept fixed. The comparison demonstrated that the HPSONN is a useful tool for training ANN, which converges quickly towards the optimal position, and can avoid overfitting in some extent.
CC 1-3 (Pharmacology)
IT 6576-51-8 118438-45-2 132244-47-4 132268-26-9 132268-27-0
177409-19-7 177409-26-6 177409-27-7 177409-30-2 177409-42-6
177409-48-2 177409-55-1 177409-56-2 182691-95-8 187802-29-5
187802-31-9 191214-23-0 194482-64-9 194482-65-0 194482-73-0
194482-74-1 194482-75-2 194482-76-3 194482-77-4 194482-78-5
194482-79-6 194482-84-3 194483-17-5 199462-84-5 199462-96-9
203114-20-9 203114-22-1 203114-23-2 203114-24-3 203114-25-4
203118-13-2 ***203118-15-4*** 203118-22-3 203118-29-0
203258-30-4 203258-32-6 203258-34-8 203258-36-0 203258-38-2
203258-42-8 203258-45-1 207845-43-0 207845-50-9 207845-51-0
207845-52-1 223437-34-1 223437-42-1 223437-47-6 245046-42-8
245046-44-0 245358-69-4 288153-08-2 561318-58-9 561318-59-0
561318-60-3 561318-61-4 561318-62-5 561318-63-6 561318-64-7
561318-65-8 561318-66-9 797060-04-9 797060-05-0 797060-06-1
797060-07-2
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hybridized particle swarm algorithm for adaptive structure training of multilayer feed-forward neural network and QSAR studies of bioactivity of organic compds.)

IT *203118-15-4*
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hybridized particle swarm algorithm for adaptive structure training of multilayer feed-forward neural network and QSAR studies of bioactivity of organic compds.)
RN 203118-15-4 CAPLUS
CN 1H-Pyrrole-2-carboxamide, N-[5-[[(3-amino-3-iminopropyl)amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-4-[[[4-[[4-[bis(2-chloroethyl)amino]-3-fluorobenzoyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



● HCl

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L86 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:353274 CAPLUS
DOCUMENT NUMBER: 136:363862

TITLE: Composition comprising: ***serotonin*** receptor antagonists (***5HT***-2, ***5HT***-3) and agonist (***5HT***-4)
INVENTOR(S): Skogvall, Staffan
PATENT ASSIGNEE(S): Respiratorius A.B., Swed.
SOURCE: PCT Int. Appl., 160 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002036113	A1	20020510	WO 2001-SE2372	20011030
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002012888	A5	20020515	AU 2002-12888	20011030
PRIORITY APPLN. INFO.:			SE 2000-3995 A	20001101
			US 2000-244661P P	20001101
			WO 2001-SE2372 W	20011030

AB A composition comprising a combination of (a) at least one compound with agonist activity to the ***5-HT4*** receptor, (b) at least one compound with antagonist activity to the ***5-HT3*** receptor, and (c) at least one compound with antagonist activity to the ***5-HT2*** receptor is described. The invention relates to the use of said composition as a medicament for therapeutic or prophylactic treatment of disorders involving airway constriction in humans or animals.

IC ICM A61K031-395
ICS A61K031-4045; A61P011-06; A61P011-08
CC 1-11 (Pharmacology)
ST ***serotonin*** receptor agonist antagonist airway constriction treatment
IT ***5-HT*** antagonists
(***5-HT2***; composition comprising ***5-HT2*** and ***5-HT3*** ***serotonin*** receptor antagonists and ***5-HT4*** agonist as medicament for treatment of disorders involving airway constriction)
IT ***5-HT*** antagonists
(***5-HT3***; composition comprising ***5-HT2*** and ***5-HT3*** ***serotonin*** receptor antagonists and ***5-HT4*** agonist as medicament for treatment of disorders involving airway constriction)
IT ***5-HT*** agonists
(***5-HT4***; composition comprising ***5-HT2*** and ***5-HT3*** ***serotonin*** receptor antagonists and ***5-HT4*** agonist as medicament for treatment of disorders involving airway constriction)
IT Bronchi, disease
Inflammation
(chronic bronchitis; composition comprising ***5-HT2*** and

5-HT3 serotonin receptor antagonists and *5-HT4* agonist as medicament for treatment of disorders involving airway constriction)

IT Lung, disease
(chronic obstructive pulmonary disease; composition comprising *5-HT2* and *5-HT3 serotonin* receptor antagonists and *5-HT4* agonist as medicament for treatment of disorders involving airway constriction)

IT Antiasthmatics
Drug interactions
Emphysema
(composition comprising *5-HT2* and *5-HT3 serotonin* receptor antagonists and *5-HT4* agonist as medicament for treatment of disorders involving airway constriction)

IT *5-HT* receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type *5-HT2*; composition comprising *5-HT2* and *5-HT3 serotonin* receptor antagonists and *5-HT4* agonist as medicament for treatment of disorders involving airway constriction)

IT *5-HT* receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type *5-HT3*; composition comprising *5-HT2* and *5-HT3 serotonin* receptor antagonists and *5-HT4* agonist as medicament for treatment of disorders involving airway constriction)

IT *5-HT* receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type *5-HT4*; composition comprising *5-HT2* and *5-HT3 serotonin* receptor antagonists and *5-HT4* agonist as medicament for treatment of disorders involving airway constriction)

IT 138559-58-7, ADR 932
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ADR 932; composition comprising *5-HT2* and *5-HT3 serotonin* receptor antagonists and *5-HT4* agonist as medicament for treatment of disorders involving airway constriction)

IT 178485-02-4, ALEPH 2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ALEPH 2; composition comprising *5-HT2* and *5-HT3 serotonin* receptor antagonists and *5-HT4* agonist as medicament for treatment of disorders involving airway constriction)

IT 150527-36-9, FG 5974
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(FG 5974; composition comprising *5-HT2* and *5-HT3 serotonin* receptor antagonists and *5-HT4* agonist as medicament for treatment of disorders involving airway constriction)

IT 116684-57-2, GR 67330
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GR 67330; composition comprising *5-HT2* and *5-HT3 serotonin* receptor antagonists and *5-HT4* agonist as medicament for treatment of disorders involving

airway constriction)

IT 148014-93-1, KB 6933
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(KB 6933; composition comprising *5-HT2* and *5-HT3 serotonin* receptor antagonists and *5-HT4* agonist as medicament for treatment of disorders involving airway constriction)

IT 145970-12-3, KF 20170
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(KF 20170; composition comprising *5-HT2* and *5-HT3 serotonin* receptor antagonists and *5-HT4* agonist as medicament for treatment of disorders involving airway constriction)

IT 153415-44-2, LEK 8804
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LEK 8804; composition comprising *5-HT2* and *5-HT3 serotonin* receptor antagonists and *5-HT4* agonist as medicament for treatment of disorders involving airway constriction)

IT 107007-94-3, LY 211000
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LY 211000; composition comprising *5-HT2* and *5-HT3 serotonin* receptor antagonists and *5-HT4* agonist as medicament for treatment of disorders involving airway constriction)

IT 143257-98-1, Lerisetron
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Lerisetron; composition comprising *5-HT2* and *5-HT3 serotonin* receptor antagonists and *5-HT4* agonist as medicament for treatment of disorders involving airway constriction)

IT 160472-97-9, N 3389
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(N 3389; composition comprising *5-HT2* and *5-HT3 serotonin* receptor antagonists and *5-HT4* agonist as medicament for treatment of disorders involving airway constriction)

IT 161362-69-2, RS 67532
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RS 67532; composition comprising *5-HT2* and *5-HT3 serotonin* receptor antagonists and *5-HT4* agonist as medicament for treatment of disorders involving airway constriction)

IT 175413-81-7, SB 205149
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SB 205149; composition comprising *5-HT2* and *5-HT3 serotonin* receptor antagonists and *5-HT4* agonist as medicament for treatment of disorders involving airway constriction)

IT 169789-38-2, SDZ 216-454
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(SDZ 216-454; composition comprising *5-HT2* and *5-HT3 serotonin* receptor antagonists and *5-HT4* agonist as medicament for treatment of disorders involving airway constriction)

IT 148611-75-0, WAY-SEC 579
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(WAY-SEC 579; composition comprising *5-HT2* and *5-HT3 serotonin* receptor antagonists and *5-HT4* agonist as medicament for treatment of disorders involving airway constriction)

IT 21867-64-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aryl derivs.; composition comprising *5-HT2* and *5-HT3 serotonin* receptor antagonists and *5-HT4* agonist as medicament for treatment of disorders involving airway constriction)

IT 50-37-3, LSD 50-48-6, Amitriptyline 50-49-7, Imipramine 50-52-2, Thioridazine 50-53-3, Chlorpromazine, biological studies 50-67-9, *5-HT*, biological studies 55-45-8 58-38-8, Prochlorperazine 58-39-9, Perphenazine 60-87-7, Promethazine 69-23-8, Fluphenazine 84-02-6, Stemetil 91-84-9, Mepyramine 93-65-2, MCPP 102-02-3, Phenylbiguanide 117-89-5, Trifluoperazine 129-03-3, Cyproheptadine 304-52-9 361-37-5 364-62-5, Metoclopramide 486-74-8D, Quinoline-4-carboxylic acid, derivs. 487-93-4, Bufotenine 510-74-7, AMI-193 548-43-6, Elymoclavine 548-73-2, Droperidol 608-07-1, 5-Methoxytryptamine 749-02-0, Spiperone 1019-45-0 1166-34-3, Cinanserin 1977-10-2, Loxapine 2851-12-9D, derivs. 3040-44-6D, 1-Piperidineethanol, arylcarbamate derivs. 3546-03-0, Cyamemazine 4205-90-7, Clonidine 4774-24-7, Quipazine 5560-72-5, Iprindole 5786-21-0 6104-71-8, N-Desmethylclozapine 6480-67-7D, Quinoline-3-carboxamide, derivs. 7206-70-4D, derivs. 7206-70-4D, 4-Amino-5-chloro-2-methoxybenzoic acid, esters 15532-75-9, TFMPP 15574-96-6, Pizotifen 15676-16-1, Sulpiride 16357-59-8, N-Ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline 17692-51-2, Metergoline 20980-22-7D, 1-(2-Pyrimidinyl)piperazine, derivs. 21236-55-5, QX 222 23210-56-2, Ifenprodil 24190-74-7D, derivs. 24219-97-4, Mianserin 28614-26-8, N-Methylquipazine 31363-74-3, 5,7-Dihydroxytryptamine 32359-34-5, Medifoxamine 39133-31-8, Trimebutine 39478-62-1 40796-97-2, Bemesetron 42399-41-7, Diltiazem 43135-91-7D, Benzimidazolone, derivs. 54504-71-1, ML-1035 54739-18-3, Fluvoxamine 54910-89-3, Fluoxetine 55905-53-8, Clebopride 57260-68-1D, derivs. 57818-92-5, TMB 8 59729-33-8, Citalopram 60634-51-7, LY 53857 61869-08-7, Paroxetine 63758-79-2, Indalpine 64022-27-1, MK 212 64097-94-5 64795-35-3, Mesulergine 66564-14-5, Cinitapride 68696-79-7D, derivs. 74050-98-9, Ketanserin 74885-09-9 75272-39-8, YM-09151 75444-65-4, Pirenperone 75558-90-6, Amperozide 76272-78-1, BRL 24682 78263-90-8, 2-*Methylserotonin* 78950-78-4, 8-Hydroxy-2-dipropylaminotetralin 79617-96-2, Sertraline 81098-60-4, Cisapride 83366-66-9, Nefazodone 84225-95-6, Raclopride 84625-59-2, Dotarizine 85273-96-7, ICI 169369 85650-52-8, Mirtazapine 86811-09-8, Litoxetine 87051-43-2, Ritanserin 89565-68-4, Tropisetron 89565-96-8, SDZ 206-830 89771-28-8, SDZ 206-792 90182-92-6, Zacopride 99390-76-8, BRL 20627 99444-89-0, SDZ 210-204 99614-01-4, GR 38032F 99614-02-5, Ondansetron 99746-68-6, (R,R)-LY-53857 99746-70-0, (S,R)-LY-53857 99746-72-2, (R,S)-LY-53857 100648-19-9, RU 28253 100746-36-9, CGS 18102A 100762-72-9, (S,S)-LY-53857 101626-70-4, Talipexole 102670-46-2, Batanopride 106243-16-7, Thioperamide 106266-06-2, Risperidone 106469-51-6, BIM 107008-28-6, RU 24969

109216-57-1, LY 258458 109216-58-2, LY 278584 109216-59-3, LY 278989
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117086-68-7, BRL 46470 120357-05-3 120444-71-5, Deramciclane
120635-74-7, Cilansetron 120713-18-0, BMY 33462 121588-75-8,
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123441-85-0, (R)-Zacopride 123482-22-4, Zatosetron 123805-17-4, ADR
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6236 127595-43-1, BIMU 1 127618-28-4, DAU 6215 127625-29-0,
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128486-54-4, Lurosetron 129137-93-5D, derivs. 129295-19-8, AS-5370
129299-90-7, FK 1052 130580-02-8, SR 46349B 131012-61-8 132036-88-5,
Ramosetron 132539-06-1, Olanzapine 133364-63-3, DV 7028 134296-40-5,
BIMU 8 134401-97-1D, 2,3-Dihydrobenzofuran-7-carboxamide, derivs.
135729-55-4, RS 42358-197 135729-61-2, Palonosetron 135905-89-4,
Mirisetron 136013-69-9, WAY 100289 136174-04-4, RG 12915
136861-96-6, MDL 28133A 137328-52-0, LY 215840 138752-34-8, RS 56532
139094-48-7, KF 18259 139290-65-6, MDL 100907 139290-69-0, MDL 100151
140865-88-9, BRL 46470A 141034-42-6, DAT 582 141196-99-8, SC-53116
141533-35-9, SDZ 216-525 ***142228-17-9***, TKS 159 143137-35-3, RS
56812 143137-37-5, RS-056812-198 143178-84-1, MDL 72699 143381-68-4,
ADR-882 143407-29-8, Iodophenpropit 144625-51-4, GR 113808
145082-87-7, KF 17643 146388-57-0, SC-49518 146714-97-8, WAY 100635
146715-07-3, Desmethyl-WAY 100635 147600-74-6, SC-52491 148565-09-7,
KB-R 6933 148702-58-3, SB 204070 148868-55-7, ML 10302 149409-57-4,
NE-100 149685-78-9 149685-89-2 149719-06-2, RS 23597 153608-99-2,
KAE-393 155106-73-3, VB20B7 160599-89-3, VA21B7 161178-10-5, YM 992
162413-52-7, GK 128 166743-12-0, SK-951 166815-18-5, RS 17017
167933-07-5, BIMT 17 168986-60-5, RS 67333 168986-61-6, RS 67506
172679-55-9, SR 59768 173339-89-4, Y-34959 179474-81-8, Prucalopride
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RS 57639 202590-69-0, (+)-Norcisapride 202590-69-0D, derivs.
207605-20-7 208661-17-0, LU 111995 217635-62-6 217635-64-8
220850-98-6, YM-53389 303953-05-1 303953-06-2 303955-07-9, YM-47813
380847-59-6D, derivs. 380847-60-9D, derivs. 380847-61-0D, derivs.
380847-66-5 380893-13-0, BRL 47204 380893-14-1, CP-93318
380893-15-2, GYKI-48903 380893-16-3, KB-6922 380893-18-5, N-3256
380893-19-6, ONO-3051 380893-20-9, RS-25259 380893-21-0, SDZ 210-205
380893-22-1, SDZ 214-322 380893-23-2, SDZ 322 380893-25-4, Y 2513
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(composition comprising ***5-HT2*** and ***5-HT3 serotonin*** receptor antagonists and ***5-HT4*** agonist as medicament for treatment of disorders involving airway constriction)

IT 380893-26-5, SEC 579 422506-75-0D, derivs. 422506-76-1D, derivs.
422506-77-2 422509-62-4D, derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(composition comprising ***5-HT2*** and ***5-HT3 serotonin*** receptor antagonists and ***5-HT4*** agonist as medicament for treatment of disorders involving airway constriction)

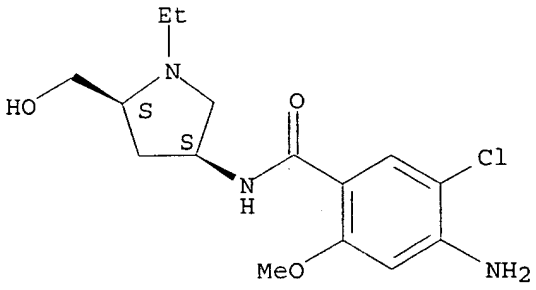
IT ***142228-17-9***, TKS 159
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(composition comprising *5-HT2* and *5-HT3 serotonin* receptor antagonists and *5-HT4* agonist as medicament for treatment of disorders involving airway constriction)

RN 142228-17-9 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L86 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:923608 CAPLUS

DOCUMENT NUMBER: 136:31700

TITLE: A composition comprising a combination of *5-HT4* receptor agonists and *5-HT3* receptor antagonists for treatment of disorders involving airway constriction

INVENTOR(S): Skogvall, Staffan

PATENT ASSIGNEE(S): Respiratorius AB, Swed.

SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001095902	A1	20011220	WO 2000-SE2612	20001220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001025663	A5	20011224	AU 2001-25663	20001220
EP 1302204	A1	20030416	EP 2001-610108	20011015
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.:

SE 2000-1267	A	20000615
WO 2000-SE1267	A	20000615
WO 2000-SE2612	W	20001220

AB The present invention relates to a composition comprising a combination of (a) at least one compound with agonist activity to the *5-HT4*

receptor and (b) at least one compound with antagonist activity to the *5-HT3* receptor and to the use of said compound in the manufacture of a medicament for therapeutic or prophylactic treatment of disorders involving airway constriction of a human or animal body, as well as methods of treatment, wherein said compds. are administered.

IC A61K031-395; A61K031-4045; A61P011-06; A61P011-08

CC 1-9 (Pharmacology)

ST airway constriction disorder HT receptor agonist antagonist; *serotonin* receptor agonist antagonist airway constriction disorder

IT *5-HT* antagonists
(*5-HT3*; composition comprising a combination of *5-HT4* receptor agonists and *5-HT3* receptor antagonists for treatment of disorders involving airway constriction)

IT *5-HT* agonists
(*5-HT4*; composition comprising a combination of *5-HT4* receptor agonists and *5-HT3* receptor antagonists for treatment of disorders involving airway constriction)

IT Bronchodilators
Drug interactions
(composition comprising a combination of *5-HT4* receptor agonists and *5-HT3* receptor antagonists for treatment of disorders involving airway constriction)

IT Respiratory system, disease
(pathol. constriction; composition comprising a combination of *5-HT4* receptor agonists and *5-HT3* receptor antagonists for treatment of disorders involving airway constriction)

IT Muscle relaxants
(smooth; composition comprising a combination of *5-HT4* receptor agonists and *5-HT3* receptor antagonists for treatment of disorders involving airway constriction)

IT *5-HT* receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type *5-HT3*; composition comprising a combination of *5-HT4* receptor agonists and *5-HT3* receptor antagonists for treatment of disorders involving airway constriction)

IT *5-HT* receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type *5-HT4*; composition comprising a combination of *5-HT4* receptor agonists and *5-HT3* receptor antagonists for treatment of disorders involving airway constriction)

IT 148014-93-1, KB 6933
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(KB 6933; composition comprising a combination of *5-HT4* receptor agonists and *5-HT3* receptor antagonists for treatment of disorders involving airway constriction)

IT 107007-94-3, LY 211000
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LY 211000; composition comprising a combination of *5-HT4* receptor agonists and *5-HT3* receptor antagonists for treatment of disorders involving airway constriction)

IT 169789-38-2, SDZ 216-454
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SDZ 216-454; composition comprising a combination of *5-*

HT4 receptor agonists and *5-HT3* receptor antagonists for treatment of disorders involving airway constriction)

IT 50-48-6, Amitriptyline 50-49-7, Imipramine 50-53-3, Chlorpromazine, biological studies 50-67-9, ***Serotonin***, biological studies 51-17-2D, Benzimidazole, 2-piperidinmethyl ethers 55-45-8 58-38-8, Prochlorperazine 58-39-9, Perphenazine 69-23-8, Fluphenazine 91-84-9, Mepyramine 93-65-2, MCPP 102-02-3, Phenylbiguanide 117-89-5, Trifluoperazine 129-03-3, Cyproheptadine 304-52-9 361-37-5 364-62-5, Metoclopramide 480-91-1D, derivs. 487-93-4, Bufotenine 548-73-2, Droperidol 608-07-1, 5-Methoxytryptamine 3040-44-6D, 1-Piperidine ethanol, arylcarbamate derivs. 3546-03-0, Cyamemazine 4774-24-7, Quipazine 5786-21-0 7206-70-4D, derivs. 7206-70-4D, 4-Amino-5-chloro-2-methoxybenzoic acid, esters 15532-75-9, TFMPP 15574-96-6, Pizotifen 17692-51-2, Metergoline 21236-55-5, QX 222 23210-56-2, Ifenprodil 24190-74-7D, 4-Amino-5-chloro-2-methoxy benzamide, derivs. 24219-97-4, Mianserin 28614-26-8, N-Methylquipazine 39133-31-8, Trimebutine 39478-62-1 40796-97-2, MDL 72222 42399-41-7, Diltiazem 54504-71-1, ML-1035 55745-83-0D, derivs. 55905-53-8, Clebopride 57818-92-5, TMB 8 63758-79-2, Indalpine 64022-27-1, MK 212 64097-94-5 66564-14-5, Cinitapride 68696-79-7D, derivs. 74050-98-9, Ketanserin 74885-09-9, 5-Carboxamidotryptamine 75272-39-8, YM-09151 76272-78-1, BRL 24682 78263-90-8, 2-***Methylserotonin*** 78950-78-4, 8-Hydroxy-2-dipropylaminotetralin 81098-60-4, Cisapride 85650-52-8, Mirtazapine 86811-09-8, Litoxetine 87051-43-2, Ritanserin 89565-68-4, ICS 205930 89565-96-8, SDZ 206-830 89771-28-8, SDZ 206-792 90182-92-6, Zacopride 98330-05-3, Anpirtoline 99390-76-8, BRL 20627 99444-89-0, SDZ 210-204 99614-01-4, GR 38032F 99614-02-5, Ondansetron 100648-19-9, RU 28253 101626-70-4, Talipexole 102670-46-2, Batanopride 106243-16-7, Thioperamide 106469-51-6, CF 109203 107008-28-6, RU 24969 109216-57-1, LY 258458 109216-58-2, LY 278584 109216-59-3, LY 278989 109872-41-5, BRL 24924 109889-09-0, BRL 43694 111628-39-8D, derivs. 112727-80-7, Renzapride 112885-41-3, Mosapride 113140-33-3, GR 65630 115338-32-4, NAN-190 115626-53-4, QICS 205-930 115753-79-2, Galanolactone 115956-12-2, Dolasetron 115956-13-3, Dolasetron mesylate 116356-96-8D, Thiophene carboxamide, derivs. 116684-57-2, GR 67330 116684-92-5, Galdansetron 117086-68-7, BRL 46470 120635-74-7, Cilansetron 120713-18-0, BMY 33462 121650-80-4, Pancopride 122852-42-0, Alosetron 122866-79-9, R076186 123040-69-7, Azasetron 123258-84-4, Itasetron 123441-85-0, (R)-Zacopride 123482-22-4, Zatosetron 123805-17-4, ADR 851 127595-11-3, DAU 6236 127595-43-1, BIMU 1 127618-28-4, DAU 6215 127625-29-0, RP 62203 128200-30-6, L-683877 128292-55-7, (-)-Zacopride 128486-54-4, Lurosetron 129295-19-8, AS-5370 129299-90-7, FK 1052 131012-61-8 132036-88-5, Ramosetron 134296-40-5, BIMU 8 135729-55-4, RS 42358-197 135729-61-2, Palonosetron 135729-62-3, RS-25259-197 135905-89-4, Mirisetron 136013-69-9, WAY 100289 136174-04-4, RG 12915 138559-58-7, ADR 932 138682-46-9D, derivs. 138752-34-8, RS 56532 139094-48-7, KF 18259 140865-88-9, BRL 46470A 141034-42-6, DAT 582 141196-99-8, SC-53116 141533-35-9, SDZ 216-525 ***142228-17-9***, TKS 159 143137-35-3, RS 56812 143137-37-5, RS-056812-198 143178-84-1, MDL 72699 143257-98-1, Lerisetron 143381-68-4, ADR-882 143407-29-8, Iodophenpropit 144625-51-4, GR 113808 145082-87-7, KF 17643 145970-12-3 146388-57-0, SC-49518 147600-74-6, SC-52491 148565-09-7, KB-R 6933 148611-75-0, WAY-SEC 579 148702-58-3, SB 204070 148868-55-7, ML.10302 149685-78-9 149685-89-2 149719-06-2, RS 23597 153608-99-2, YM 114 155106-73-3, VB20B7 160472-97-9, N 3389 160599-89-3 161362-69-2, RS 67532 162413-52-7, GK 128 166743-12-0, SK-951 166815-18-5, RS 17017 168986-60-5, RS 67333 168986-61-6, RS 67506 172679-55-9, SR 59768 173339-89-4 174486-91-0D, derivs. 175413-81-7, SB 205149 179474-81-8, Prucalopride 179913-42-9

182808-16-8D, derivs. 189188-57-6, Zelmac 193404-36-3, RS 57639
202590-69-0, (+)-Norcisapride 207296-78-4 220850-98-6, YM-53389
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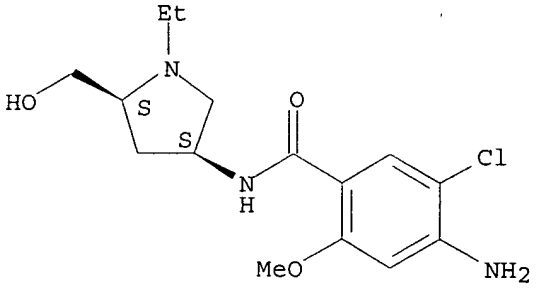
380847-61-0D, derivs. 380847-63-2 380847-64-3 380847-65-4
380847-66-5 380893-13-0, BRL 47204 380893-14-1, CP 93318
380893-15-2, GYKI 48903 380893-16-3, KB 6922 380893-18-5, N 3256
380893-19-6, ONO 3051 380893-20-9, RS 25259 380893-21-0, SDZ 210-205
380893-22-1, SDZ 214-322 380893-23-2, SDZ 322 380893-25-4, Y 2513
380893-26-5, SEC 579
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition comprising a combination of ***5-HT4*** receptor agonists and ***5-HT3*** receptor antagonists for treatment of disorders involving airway constriction)

IT ***142228-17-9***, TKS 159
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition comprising a combination of ***5-HT4*** receptor agonists and ***5-HT3*** receptor antagonists for treatment of disorders involving airway constriction)

RN 142228-17-9 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L86 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:900443 CAPLUS
DOCUMENT NUMBER: 134:51395
TITLE: ***5-HT4*** receptor agonists and ***5-HT3*** receptor antagonists for treatment of bronchocontraction
INVENTOR(S): Skogvall, Staffan
PATENT ASSIGNEE(S): Respiratorius Ab, Swed.
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000076500	A2	20001221	WO 2000-SE1267	20000615
WO 2000076500	A3	20010712		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

WO 2000064441	A2	20001102	WO 2000-SE819	20000428
WO 2000064441	A3	20010614		

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2000058619	A5	20010102	AU 2000-58619	20000615
EP 1185263	A2	20020313	EP 2000-944534	20000615

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

JP 2003501462	T2	20030114	JP 2001-502833	20000615
AU 2001025663	A5	20011224	AU 2001-25663	20001220
AU 2001025664	A5	20011224	AU 2001-25664	20001220

PRIORITY APPLN. INFO.:

SE 1999-2251	A	19990615
SE 1999-2252	A	19990615
US 1999-139632P	P	19990617
US 1999-139633P	P	19990617
WO 2000-SE819	W	20000428
SE 1999-1531	A	19990428
US 1999-131355P	P	19990428
SE 1999-1906	A	19990526
US 1999-136604P	P	19990527
WO 2000-SE1267	W	20000615
WO 2000-SE2612	W	20001220
WO 2000-SE2613	W	20001220

AB The present invention relates to a compound having agonist activity to the *5-HT4* receptor for use as a medicament and to the use of said compds. in the manufacture of a medicament for use in therapeutic or prophylactic treatment of disorders involving bronchocontraction of a human or animal body, as well as methods of treatment, wherein said compds. are administered. The present invention also relates to a compound. having antagonist activity to the *5-HT3* receptor for use as a medicament and to the use of said compound in the manufacture of a medicament for use in therapeutic or prophylactic treatment of disorders involving bronchocontraction of a human or animal body, as well as methods of treatment, wherein said compds. are administered. An example is given showing that the selective *5-HT4* receptor agonist RS 67333 gives a strong sustained relaxing effect on the spontaneous tone in human in vitro prepns.

IC ICM A61K031-4045
ICS A61P011-08; A61P011-06

CC 1-9 (Pharmacology)

ST *serotoninergic* agonist antagonist bronchodilator

IT *5-HT* antagonists

(*5-HT3*; *5-HT4* receptor agonists
and *5-HT3* receptor antagonists for treatment of
bronchocontraction)

IT Antidepressants
Bronchodilators
Psychotropics
(*5-HT4* receptor agonists and *5-*
HT3 receptor antagonists for treatment of bronchocontraction)

IT *5-HT* agonists
(*5-HT4*; *5-HT4* receptor agonists
and *5-HT3* receptor antagonists for treatment of
bronchocontraction)

IT 168986-60-5, RS 67333
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(*5-HT4* receptor agonists and *5-*
HT3 receptor antagonists for treatment of bronchocontraction)

IT 50-53-3, Chlorpromazine, biological studies 50-67-9,
5-Hydroxytryptamine, biological studies 55-45-8 58-38-8,
Prochlorperazine 58-39-9, Perphenazine 69-23-8, Fluphenazine
117-89-5, Trifluoperazine 364-62-5, Metoclopramide 487-93-4,
5-Hydroxy-N,N-dimethyltryptamine 548-73-2, Droperidol 608-07-1,
5-Methoxytryptamine 3546-03-0, Cyamemazine 4774-24-7, Quipazine
5786-21-0, Clozapine 21236-55-5, QX 222 23210-56-2, Ifenprodil
28614-26-8, N-Methylquipazine 39133-31-8, Trimebutine 39478-62-1
40796-97-2, MDL 72222 42399-41-7, Diltiazem 57818-92-5, TMB 8
64097-94-5 66564-14-5, Cinitapride 74885-09-9, 5-Carboxamidotryptamine
75272-39-8, YM-09151 76272-78-1, BRL 24682 78950-78-4,
8-Hydroxy-2-dipropylaminotetralin 81098-60-4, Cisapride 85273-96-7,
ICI 169369 85650-52-8, Mirtazapine 86811-09-8, Litoxetine
89565-68-4, ICS-205930 90182-92-6, Zacopride 98330-05-3, Anpirtoline
99390-76-8, BRL 20627 99614-02-5, GR 38032 100648-19-9, RU 28253
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BRL-43694 112727-80-7, Renzapride 112885-41-3, Mosapride
113140-33-3, GR 65630 115753-79-2, Galanolactone 115956-12-2,
Dolasetron 115956-13-3, Dolasetron mesylate 120635-74-7, Cilansetron
120713-18-0, BMY 33462 121650-80-4, Pancopride 122732-06-3
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123258-84-4, Itasetron 123441-85-0 123482-22-4, Zatosetron
125557-35-9, ML-1035 127595-11-3, DAU 6236 127595-43-1, BIMU 1
127618-28-4, Dau 6215 128200-30-6, L-683877 129299-90-7, FK 1052
132036-88-5, Ramosetron 134296-40-5, BIMU 8 135729-55-4, RS-42358-197
135729-61-2, Palonosetron 135729-62-3, RS-25259-197 136013-69-9, Way
100289 136174-04-4, RG 12915 138752-34-8, RS 56532 139094-48-7, KF
18259 140865-88-9, BRL 46470A 141034-42-6, DAT-582 141196-99-8, Sc
53116 141533-35-9, SDZ 216-525 ***142228-17-9***, TKS159
143137-35-3, RS-56812 143137-37-5, RS-056812-198 143178-84-1, MDL
72699 143381-68-4, ADR 882 143407-29-8, Iodophenpropit 145082-87-7,
KF 17643 146388-57-0, SC-49518 147600-74-6, SC-52491 148565-09-7,
KB-R 6933 148702-58-3, SB 204070 148868-55-7, ML 10302 149719-06-2,
RS 23597-190 155106-73-3, VB20B7 160599-89-3, VA 21B7 162413-52-7,
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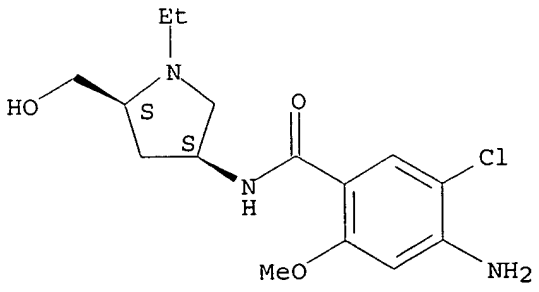
67506 172679-55-9, SR59768 179474-80-7, R093877 179474-81-8,
Prucalopride 179913-42-9 189188-57-6, Zelmac 193404-36-3, RS 57639
207605-20-7 220850-98-6, YM-53389 303955-07-9, YM-47813
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(*5-HT4* receptor agonists and *5-*
HT3 receptor antagonists for treatment of bronchocontraction)

IT 123805-17-4, ADR 851
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ADR 851; *5-HT4* receptor agonists and *5-HT3* receptor antagonists for treatment of bronchocontraction)
IT 138559-58-7, ADR 932
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ADR 932; *5-HT4* receptor agonists and *5-HT3* receptor antagonists for treatment of bronchocontraction)
IT 160472-97-9, N 3389
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(N 3389; *5-HT4* receptor agonists and *5-HT3* receptor antagonists for treatment of bronchocontraction)
IT 161362-69-2, RS 67532
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RS 67532; *5-HT4* receptor agonists and *5-HT3* receptor antagonists for treatment of bronchocontraction)
IT 175413-81-7, SB 205149
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SB 205149; *5-HT4* receptor agonists and *5-HT3* receptor antagonists for treatment of bronchocontraction)
IT 169789-38-2, SDZ 216-454
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SDZ 216-454; *5-HT4* receptor agonists and *5-HT3* receptor antagonists for treatment of bronchocontraction)
IT 99614-01-4, SN 307
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SN 307; *5-HT4* receptor agonists and *5-HT3* receptor antagonists for treatment of bronchocontraction)
IT 148611-75-0, WAY 100579
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(WAY 100579; *5-HT4* receptor agonists and *5-HT3* receptor antagonists for treatment of bronchocontraction)
IT 153608-99-2, YM 114
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(YM 114; *5-HT4* receptor agonists and *5-HT3* receptor antagonists for treatment of bronchocontraction)
IT *142228-17-9*, TKS159
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(*5-HT4* receptor agonists and *5-HT3* receptor antagonists for treatment of bronchocontraction)
RN 142228-17-9 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L86 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:772451 CAPLUS
DOCUMENT NUMBER: 133:329581
TITLE: ***Serotoninergic*** agonists and antagonists for treatment of bronchoconstriction
INVENTOR(S): Skogvall, Staffan
PATENT ASSIGNEE(S): Respiratorius AB, Swed.
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000064441	A2	20001102	WO 2000-SE819	20000428
WO 2000064441	A3	20010614		
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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EP 1173168	A2	20020123	EP 2000-937417	20000428
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JP 2002542287	T2	20021210	JP 2000-613432	20000428
WO 2000076500	A2	20001221	WO 2000-SE1267	20000615
WO 2000076500	A3	20010712		
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AU 2000058619	A5	20010102	AU 2000-58619	20000615
EP 1185263	A2	20020313	EP 2000-944534	20000615
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JP 2003501462	T2	20030114	JP 2001-502833	20000615
US 2002173505	A1	20021121	US 2001-984329	20011029

PRIORITY APPLN. INFO.:

SE 1999-1531	A	19990428
US 1999-131355P	P	19990428
SE 1999-1906	A	19990526
US 1999-136604P	P	19990527
SE 1999-2251	A	19990615
SE 1999-2252	A	19990615
US 1999-139632P	P	19990617
US 1999-139633P	P	19990617

WO 2000-SE819 W 20000428
WO 2000-SE1267 W 20000615

AB The present invention relates to a compound having agonist activity to the ***5-HT4*** receptor or antagonist activity to the ***5-HT2a*** receptor and manufacture of a medicament for prophylactic or therapeutic treatment of disorders involving bronchoconstriction of a human or animal, such as asthma, emphysema, chronic bronchitis, chronic obstructive pulmonary disease, depression, anorectic or bulimic eating disorders, anxiety or various psychotic conditions including schizophrenia. Compds. of the present invention have the capacity of reducing the pathol. bronchoconstriction by at least 30%, preferably at least 60%, and most preferably at least 90%.

IC ICM A61K031-395

CC 1-7 (Pharmacology)
Section cross-reference(s): 63

ST ***serotoninergic*** agonist antagonist bronchoconstriction; antiasthmatic ***serotoninergic*** agonist antagonist; antidepressant ***serotoninergic*** agonist antagonist; anxiolytic ***serotoninergic*** agonist antagonist; antipsychotic ***serotoninergic*** agonist antagonist

IT ***5-HT*** antagonists
(***5-HT2A***; ***serotoninergic*** agonists and antagonists for treatment of bronchoconstriction-related disorders)

IT ***5-HT*** agonists
(***5-HT4***; ***serotoninergic*** agonists and antagonists for treatment of bronchoconstriction-related disorders)

IT Bronchi
(bronchoconstriction; ***serotoninergic*** agonists and antagonists for treatment of bronchoconstriction-related disorders)

IT Appetite
(bulimia; ***serotoninergic*** agonists and antagonists for treatment of bronchoconstriction-related disorders)

IT Bronchi
(chronic bronchitis; ***serotoninergic*** agonists and antagonists for treatment of bronchoconstriction-related disorders)

IT Lung, disease
(chronic obstructive; ***serotoninergic*** agonists and antagonists for treatment of bronchoconstriction-related disorders)

IT Anorexia
Antiasthmatics
Antidepressants
Antipsychotics
Anxiolytics
Bronchodilators
Drug delivery systems
Emphysema
Schizophrenia
(***serotoninergic*** agonists and antagonists for treatment of bronchoconstriction-related disorders)

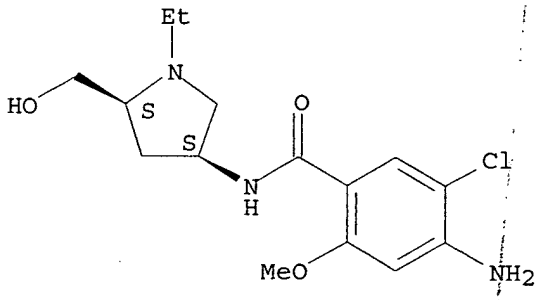
IT 50-37-3, LSD 50-49-7, Imipramine 50-67-9D, ***Serotonin***, derivs. 110-85-0D, Piperazine, aryl derivs., biological studies 129-03-3, Cyproheptadine 361-37-5, Methysergide 364-62-5, Metoclopramide 487-93-4, 5-Hydroxy-N,N-dimethyltryptamine 510-74-7, AMI-193 548-43-6, Elymoclavine 608-07-1, 5-Methoxytryptamine 749-02-0, Spiperone 4205-90-7, Clonidine 5560-72-5, Iprindole 15574-96-6, Pizotifen 16357-59-8, N-Ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline 17692-51-2, Metergoline 20980-22-7D, 1-(2-Pyrimidinyl)piperazine, derivs. 24219-97-4, Mianserin 28299-33-4D, Imidazoline, aryloxyalkyl derivs. 32359-34-5, Medifoxamine 32896-53-0, LY 53857 free base 54739-18-3, Fluvoxamine 54910-89-3,

Fluoxetine 59729-33-8, Citalopram 61869-08-7, Paroxetine 64795-35-3, Mesulergine 67537-81-9D, Hexahydrocarbazole, derivs. 74050-98-9, Ketanserin 74885-09-9, 5-Carboxamidotryptamine 75272-39-8, YM 09151 75558-90-6, Amperozide 78950-78-4, 8-OH-DPAT 79617-96-2, Sertraline 81098-60-4, Cisapride 83366-66-9, Nefazodone 84225-95-6, Raclopride 84625-59-2, Dotarizine 85273-96-7, ICI 169369 87051-43-2, Ritanserin 90182-92-6, Zacopride 99614-02-5, Ondansetron 99746-68-6, (R,R)-LY-53857 99746-70-0, (S,R)-LY-53857 99746-72-2, (R,S)-LY-53857 100746-36-9, CGS 18102A 100762-72-9, (S,S)-LY-53857 106266-06-2, Risperidone 107703-78-6, MDL 11939 109872-41-5, BRL 24924 112192-04-8, Roxindole 112727-80-7, Renzapride 112885-41-3, Mosapride 112922-55-1, Cericlamine 120444-71-5, Deramciclane 121588-75-8, Amesergide 122866-79-9, R 076186 125557-35-9 125926-17-2, Sarpogrelate 127266-56-2, WY 50324 127595-11-3, DAU 6236 127595-43-1, BIMU 1 127625-29-0, Fananserin 130580-02-8, SR 46349B 132539-06-1, Olanzapine 133364-63-3, DV 7028 134296-40-5, BIMU 8 136861-96-6, MDL 28133A 137328-52-0, LY 215840 138752-34-8, RS 56532 139290-65-6, MDL 100907 139290-69-0, MDL 100151 141196-99-8, SC-53116 ***142228-17-9***, TKS 159 146388-57-0, SC-49518 146714-97-8, WAY 100635 146714-97-8D, WAY 100635, derivs. 146715-07-3, Desmethyl-WAY 100635 148702-58-3, SB 204070 148868-55-7, ML 10302 149409-57-4 150527-23-4 150527-36-9, FG5893 hydrochloride 153415-44-2 155106-73-3, VB 20B7 161178-10-5, YM 992 161362-69-2, RS 67532 166743-12-0, SK-951 166815-18-5, RS 17017 167933-07-5, BIMT 17 168986-60-5, RS 67333 168986-61-6, RS 67506 169789-38-2, SDZ 216-454 172679-55-9, SR59768 175413-81-7, SB 205149 178485-02-4, ALEPH-2 179474-80-7, R 093877 179474-81-8, Prucalopride 183949-64-6, NRA0045 189188-57-6, Zelmac 193404-36-3, RS 57639 208661-17-0, LU 111995 217635-62-6 217635-64-8 220850-98-6, YM 53389 303953-05-1 303953-06-2 303955-07-9, YM 47813
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(***serotoninergic*** agonists and antagonists for treatment of bronchoconstriction-related disorders)

IT ***142228-17-9***, TKS 159
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(***serotoninergic*** agonists and antagonists for treatment of bronchoconstriction-related disorders)

RN 142228-17-9 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L86 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:722082 CAPLUS
DOCUMENT NUMBER: 129:337877
TITLE: New ***gastroprokinetic*** agent TKS159: 4-amino-5-chloro-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]-2-methoxybenzamide
AUTHOR(S): Adachi, Tsutomu; Mizoguchi, Jun-Ichi; Hayashi, Yasuo; Yamashoji, Yuko; Kanehisa, Nobuko; Kai, Yasushi; Inoue, Yoshihisa
CORPORATE SOURCE: Res. and Dev. Dep., Teikoku Chem. Industries Co. Ltd, Hyogo, 664, Japan
SOURCE: Acta Crystallographica, Section C: Crystal Structure Communications (1998), C54(10), 1527-1529
CODEN: ACSCEE; ISSN: 0108-2701
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The absolute configuration of the title compound (TKS159, C15H22ClN3O3) was determined Crystallog. data are given. The bent conformation of the mol., in which the aromatic and pyrrolidine rings are at nearly 60° to each other, is maintained by intra- and intermol. H bonds. A three-dimensional network of H bonds is formed among the amino, hydroxy and carbonyl groups of neighboring mols.

CC 75-8 (Crystallography and Liquid Crystals)
Section cross-reference(s): 6, 27, 63

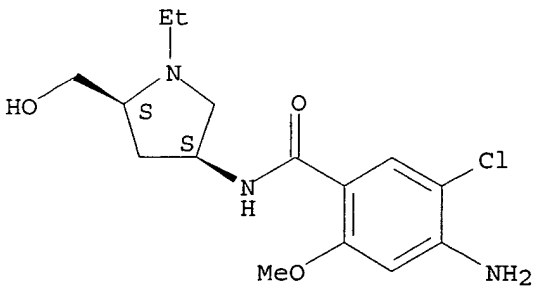
ST mol structure amino ethylhydroxymethylpyrrolidinyl methoxy benzamide; structure amino chloro ethylhydroxymethylpyrrolidinyl methoxy benzamide; ***gastroprokinetic*** agent TKS159 abs conformation structure

IT ***142228-17-9***, TKS159
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(crystal structure and absolute configuration of)

IT ***142228-17-9***, TKS159
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(crystal structure and absolute configuration of)

RN 142228-17-9 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L86 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:630754 CAPLUS
DOCUMENT NUMBER: 127:298740
TITLE: Pharmaceutical compositions
INVENTOR(S): Shii, Noritoshi; Shinoda, Masamitsu; Watanabe, Hajime; Yonetani, Akimasa
PATENT ASSIGNEE(S): Teikoku Hormone Mfg. Co., Ltd., Japan; Takada Seiyaku K. K.
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09249561	A2	19970922	JP 1996-100693	19960315
PRIORITY APPLN. INFO.:			JP 1996-100693	19960315

AB Pharmaceutical compns. [e.g. tablets] contain 4-amino-5-chloro-2-methoxy-N-[(2S, 4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]benzamide with addition of sugar alcs., starch, monosaccharides, sucrose, stearic acid or its salts and/or talc to improve stability and bioavailability.

IC ICM A61K031-40
ICS A61K047-04; A61K047-10; A61K047-12; A61K047-26; A61K047-36; C07D207-08; C07M007-00

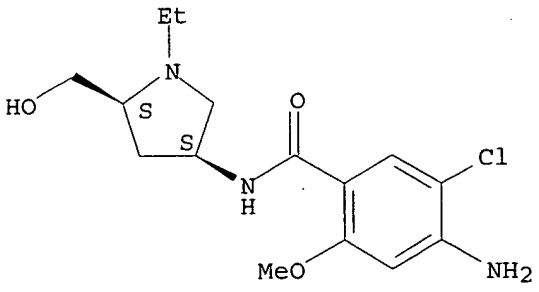
CC 63-6 (Pharmaceuticals)

IT 57-11-4, Stearic acid, biological studies 57-50-1, Sucrose, biological studies 69-65-8, Mannitol 557-04-0, Magnesium stearate 1592-23-0, Calcium stearate 9004-32-4, CM-cellulose Na salt 9005-25-8, Starch, biological studies 9005-25-8D, Starch, alphatized, biological studies 9049-76-7, HydroxypropylStarch 14807-96-6, Talc, biological studies
142228-17-9
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns.)

IT ***142228-17-9***
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns.)

RN 142228-17-9 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L86 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:20177 CAPLUS

DOCUMENT NUMBER: 128:162589
TITLE: Novel phenyl nitrogen mustard and half-mustard derivatives of distamycin A
AUTHOR(S): Cozzi, Paolo; Beria, Italo; Biasoli, Giovanni; Caldarelli, Marina; Capolongo, Laura; D'alessio, Roberto; Geroni, Cristina; Mazzini, Stefania; Ragg, Enzio; Rossi, Carla; Mongelli, Nicola
CORPORATE SOURCE: Pharmacia and Upjohn, Therapeutic Area Oncology and Immunology, Preclinical Research, Milan, 20014, Italy
SOURCE: Bioorganic & Medicinal Chemistry Letters (1997), 7(23), 2985-2990
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The design, synthesis, in vitro and in vivo activities of novel benzoyl and cinnamoyl nitrogen mustard and half-mustard derivs. of distamycin A are described and structure-activity relationships are discussed. The equipotent activities of N-ethyl-N-chloroethyl half-mustards and N,N-dichloroethyl mustards and the superior activities of cinnamoyl derivs. are the most relevant features of the series.

CC 1-6 (Pharmacology)

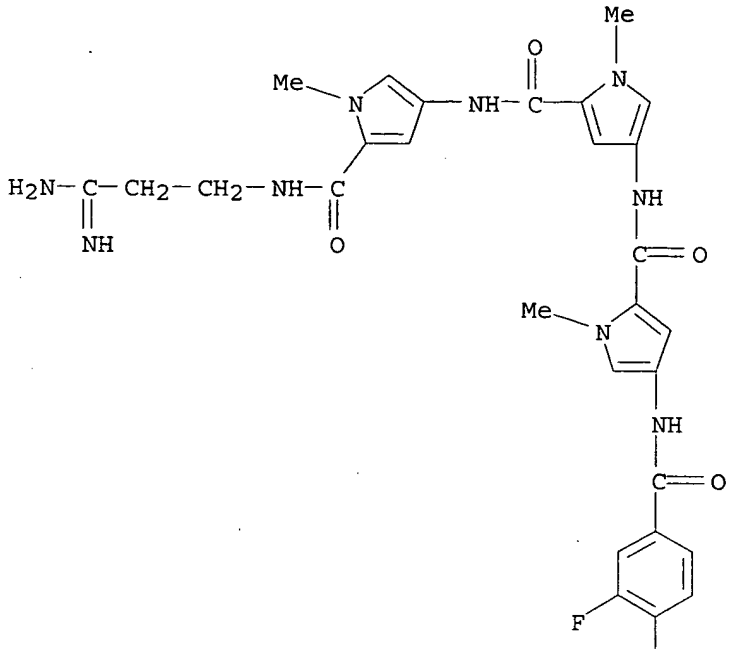
IT 118438-45-2 187802-29-5 187802-31-9 194482-64-9 194482-65-0
194482-84-3 203114-22-1 203118-05-2 203118-08-5 203118-13-2
203118-15-4 203118-21-2 203118-22-3 203118-29-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation and antitumor activity of Ph nitrogen mustard and half-mustard derivs. of distamycin A)

IT ***203118-15-4***
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation and antitumor activity of Ph nitrogen mustard and half-mustard derivs. of distamycin A)

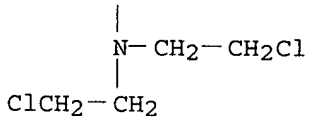
RN 203118-15-4 CAPLUS

CN 1H-Pyrrole-2-carboxamide, N-[5-[[(3-amino-3-iminopropyl)amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-4-[[[4-[[4-[bis(2-chloroethyl)amino]-3-fluorobenzoyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



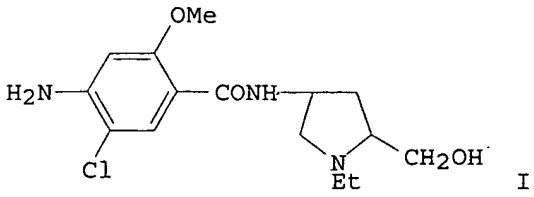
● HCl

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L86 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:586 CAPLUS
DOCUMENT NUMBER: 120:586
TITLE: Benzamide derivative for improvement of ***digestive tract*** movement
INVENTOR(S): Sakyama, Hideyo; Sekida, Mariko; Shinoda, Masamitsu; Fujiwara, Hiromichi
PATENT ASSIGNEE(S): Teikoku Hormone Mfg Co Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05229942	A2	19930907	JP 1992-88444	19920225
JP 3242975	B2	20011225		
PRIORITY APPLN. INFO.:			JP 1992-88444	19920225

GI



I

AB Improvers for ***digestive tract*** movement contain benzamide derivative I or its salts as active ingredients. I does not affect the central nervous system, thus causing no extrapyramidal syndrome, etc. Treatment of 28.0 g 4-amino-5-chloro-2-methoxybenzoic acid with 20 g (2S,4S)-4-amino-N-ethyl-2-hydroxymethylpyrrolidine, 1-hydroxy-1H-benztriazole, and DCC in CHCl3 for 14 h gave 26.3 g (2S,4S)-I, which enhanced ***digestive tract*** movement in mice and showed antiemetic activity in dogs. Film-coated tablets containing (2S,4S)-I were formulated.

IC ICM A61K031-40
ICS C07D207-14

CC 1-9 (Pharmacology)
Section cross-reference(s): 27, 63

ST benzamide improver ***digestive tract*** movement; antiemetic benzamide prepn

IT ***Digestive tract***
(movement of, improvement of, benzamide derivative for)

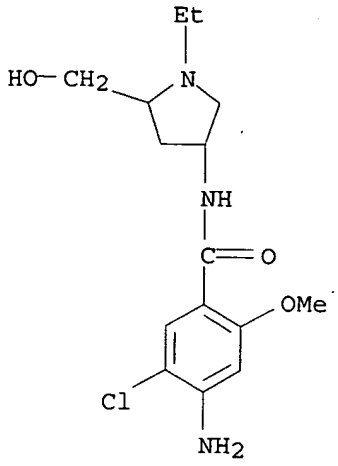
IT ***142228-16-8***
RL: BIOL (Biological study)
(***digestive tract*** movement improvement by)

IT ***142228-17-9P 142347-77-1P***
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as ***digestive tract*** movement improver and antiemetic agent)

IT ***142228-16-8***
RL: BIOL (Biological study)
(***digestive tract*** movement improvement by)

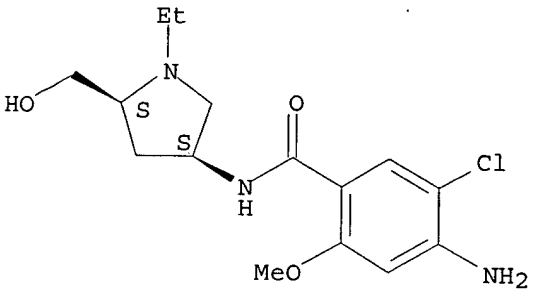
RN 142228-16-8 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)



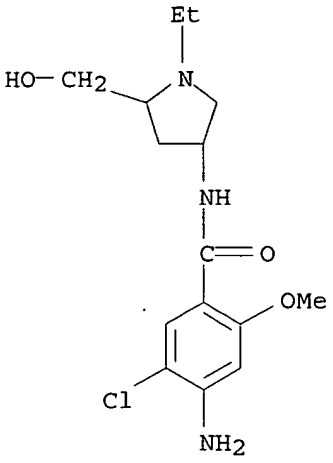
IT ***142228-17-9P 142347-77-1P***
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as ***digestive tract*** movement improver and antiemetic agent)
RN 142228-17-9 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



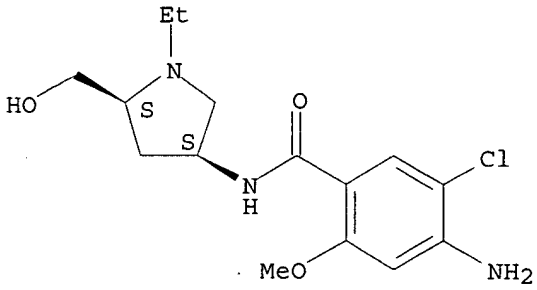
RN 142347-77-1 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride, (3S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



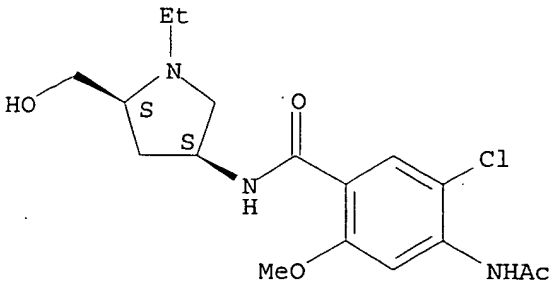
RN 142228-17-9 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



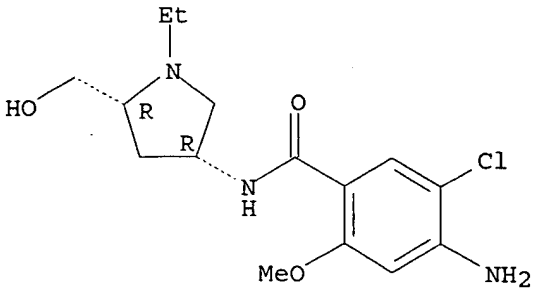
RN 142228-18-0 CAPLUS
CN Benzamide, 4-(acetylamino)-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, (3S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



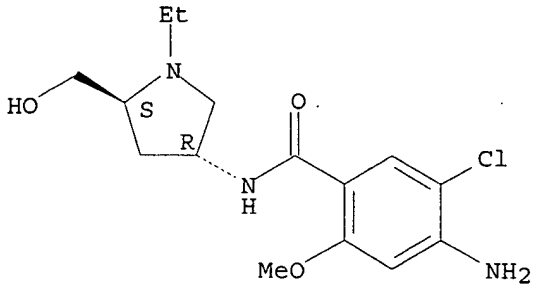
RN 142228-19-1 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[(3R,5R)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



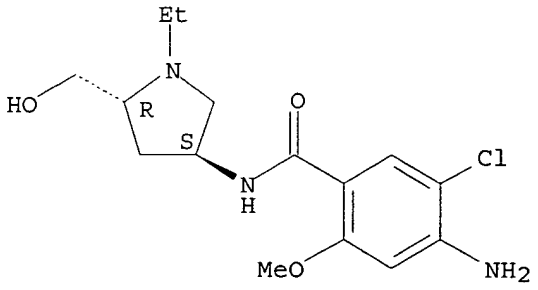
RN 142228-20-4 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[(3R,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

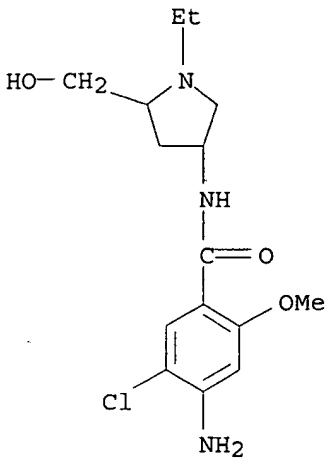


RN 142228-21-5 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[(3S,5R)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

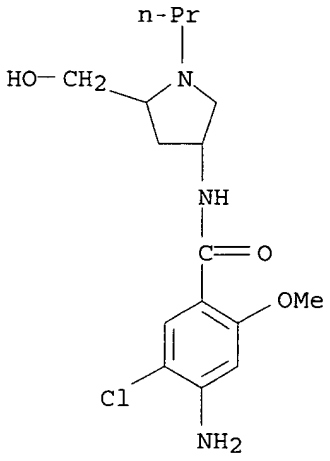


RN 142347-67-9 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



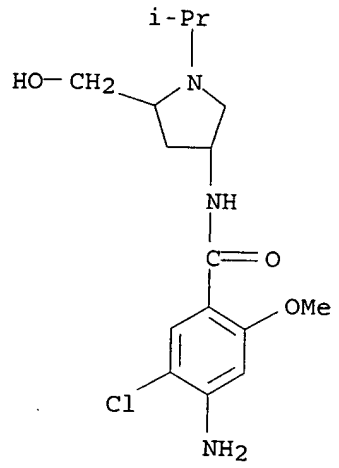
● HCl

RN 142347-68-0 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-1-propyl-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



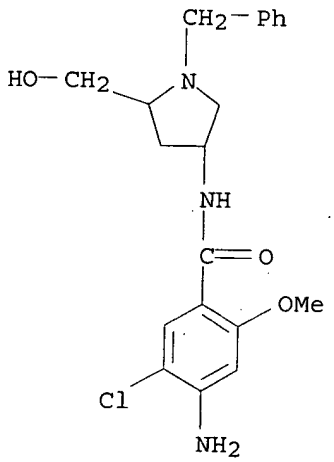
● HCl

RN 142347-69-1 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-1-(1-methylethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



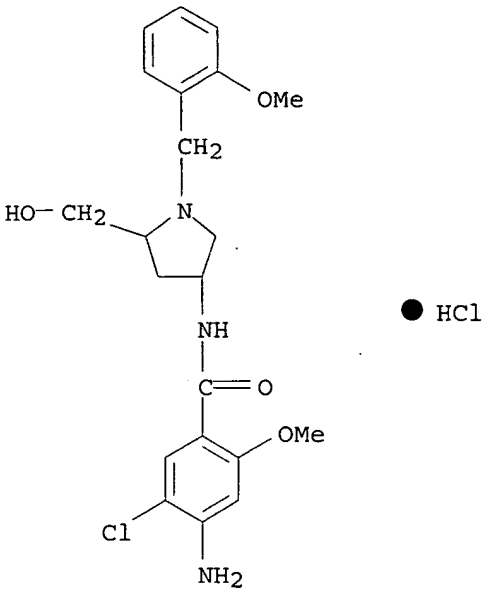
● HCl

RN 142347-70-4 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-1-(phenylmethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)

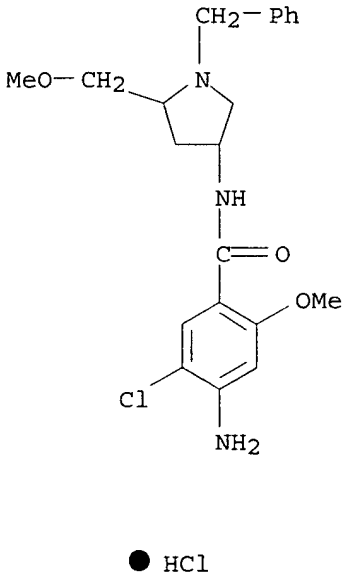


● HCl

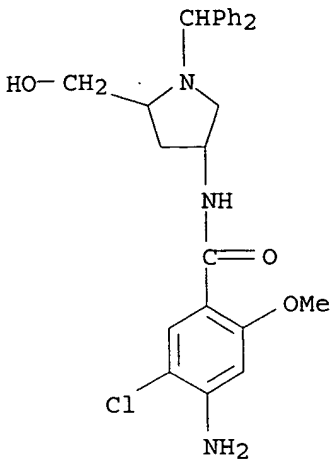
RN 142347-71-5 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-1-[(2-methoxyphenyl)methyl]-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



RN 142347-72-6 CAPLUS
CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[5-(methoxymethyl)-1-(phenylmethyl)-3-pyrrolidinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

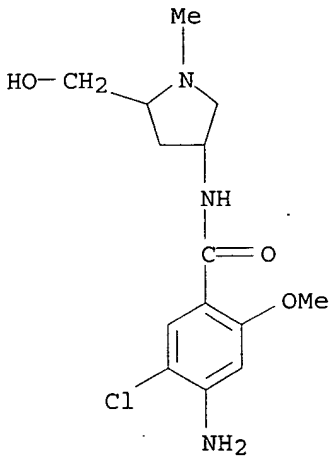


RN 142347-73-7 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[1-(diphenylmethyl)-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



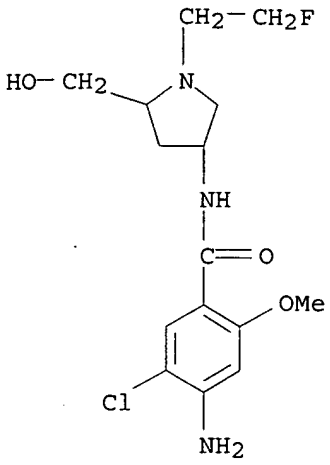
● HCl

RN 142347-74-8 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-1-methyl-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



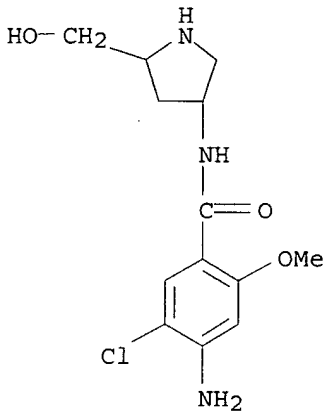
● HCl

RN 142347-75-9 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[1-(2-fluoroethyl)-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

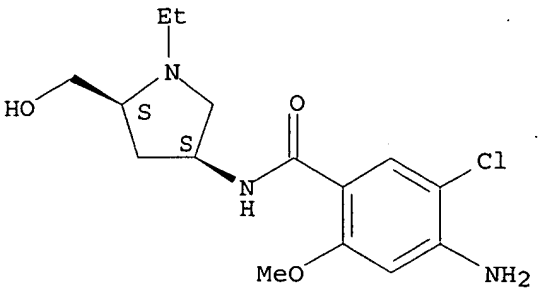
RN 142347-76-0 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 142347-77-1 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride, (3S-cis)- (9CI) (CA INDEX NAME)

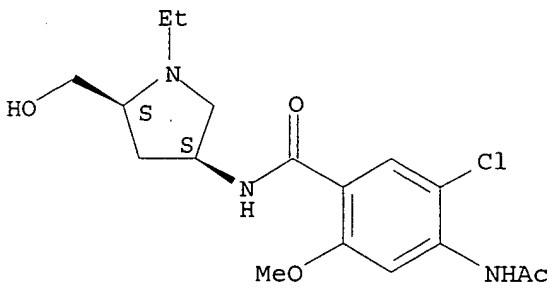
Absolute stereochemistry.



● HCl

RN 142347-78-2 CAPLUS
CN Benzamide, 4-(acetylamino)-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride, (3S-cis)- (9CI) (CA INDEX NAME)

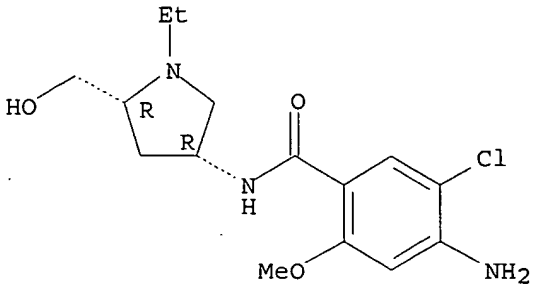
Absolute stereochemistry.



● HCl

RN 142347-79-3 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride, (3R-cis)- (9CI) (CA INDEX NAME)

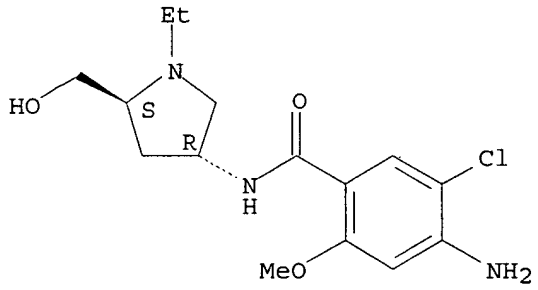
Absolute stereochemistry.



● HCl

RN 142347-80-6 CAPLUS
CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride, (3R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L86 ANSWER 16 OF 22 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1998362430 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9697104
TITLE: Effect of ***TKS159***, a novel 5-hydroxytryptamine4 agonist, on ***gastric*** contractile activity in conscious dogs.
AUTHOR: Haga N; Suzuki H; Shiba Y; Mochiki E; Mizumoto A; Itoh Z
CORPORATE SOURCE: Gastrointestinal Research Laboratory, Institute for Molecular and Cellular Regulation, Gunma University, Maebashi, Japan.
SOURCE: Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society, (1998 Aug) Vol. 10, No. 4, pp. 295-303.
Journal code: 9432572. ISSN: 1350-1925.
PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 6 Jan 1999
Last Updated on STN: 6 Jan 1999
Entered Medline: 30 Oct 1998

ABSTRACT:
A novel 5-hydroxytryptamine (***5-HT***)4 receptor agonist, ***TKS159*** , 4-amino-5-chloro-2-methoxy-N-[(2S,4S)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl] benzamide), has recently been developed as a ***gastroprokinetic*** drug. Cisapride is already used clinically to increase ***gastric*** contractions. The stimulatory effects of ***TKS159*** and cisapride on ***gastric*** contractions were examined using force transducers chronically implanted on the vagally denervated pouch (Heidenhain pouch) and the vagally innervated main ***stomach*** in conscious dogs. Contractile activity was analysed by computer and expressed as a motor index. Intravenous administration of ***TKS159*** or cisapride significantly increased the motor index in both the main ***stomach*** and the Heidenhain pouch during the fed and fasted states. Pharmacological characterization in the fasted state revealed that the contraction-stimulating activity of ***TKS159*** and cisapride on the ***stomach*** was significantly inhibited by atropine, hexamethonium and a ***5-HT4*** receptor antagonist, SDZ 205-557. Granisetron (a ***5-HT3*** receptor antagonist) significantly inhibited cisapride-induced, but not ***TKS159***-induced ***gastric*** contractions. The plasma ***motilin*** concentration was significantly increased after cisapride, but not after ***TKS159*** injection. In conclusion, ***TKS159*** has a contractile-stimulating effect on both the innervated and the denervated ***stomach.*** It is likely that a cholinergic pathway and ***5-HT4*** receptors are involved in producing the contractions, although other mechanisms cannot be excluded. Cisapride has almost the same characteristics, but the present findings suggest the involvement of ***motilin*** and ***5-HT3*** receptors in the effects of cisapride.

CONTROLLED TERM: Animals
*Cisapride: PD, pharmacology
Dogs
Drug Evaluation, Preclinical
Gastrointestinal Agents: PD, pharmacology
Gastrointestinal Motility: DE, drug effects
Motilin: AN, analysis
Muscle Contraction: DE, drug effects
*Pyrrolidines: PD, pharmacology
Serotonin Agonists: PD, pharmacology
Stimulation, Chemical
Stomach: DE, drug effects
Stomach: IR, innervation
Transducers
Vagus Nerve: DE, drug effects

CAS REGISTRY NO.: ***52906-92-0 (Motilin)***; 81098-60-4 (Cisapride)
CHEMICAL NAME: 0 (***Gastrointestinal*** Agents); 0 (Pyrrolidines); 0 (***Serotonin*** Agonists); 0 (***TKS 159***)

L86 ANSWER 17 OF 22 EMBASE
ACCESSION NUMBER: 2003052515 EMBASE
TITLE: ***5-HT***(4)receptor ligands: Applications and new prospects.

AUTHOR: Langlois M.; Fischmeister R.
CORPORATE SOURCE: M. Langlois, CNRS-BIOCIS (UPRES A 8076), Faculte de Pharmacie, F-92296 Chatenay-Malabry Cedex, France. zacopride@aol.com
SOURCE: Journal of Medicinal Chemistry, (30 Jan 2003) Vol. 46, No. 3, pp. 319-344. .
Refs: 261
ISSN: 0022-2623 CODEN: JMCMAR
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Feb 2004
Last Updated on STN: 20 Feb 2004
CONTROLLED TERM: Medical Descriptors:
*drug mechanism
drug effect
drug activity
drug structure
structure activity relation
drug potency
drug determination
drug synthesis
stomach motility
drug receptor binding
receptor affinity
stereochemistry
drug selectivity
drug bioavailability
pharmacophore
binding site
protein localization
cardiovascular system
heart arrhythmia: SI, side effect
tachycardia: SI, side effect
long QT syndrome: SI, side effect
torsade des pointes: SI, side effect
Herxheimer reaction: SI, side effect
behavior
cognition
memory
Alzheimer disease
adrenal gland
human
nonhuman
review
CONTROLLED TERM: Drug Descriptors:
serotonin 4 antagonist: AN, drug analysis
serotonin 4 antagonist: CM, drug comparison
serotonin 4 antagonist: DV, drug development
serotonin 4 antagonist: PK, pharmacokinetics
serotonin 4 antagonist: PD, pharmacology
serotonin 4 antagonist: PO, oral drug administration
serotonin 4 agonist: AE, adverse drug reaction
serotonin 4 agonist: AN, drug analysis

serotonin 4 agonist: CM, drug comparison
serotonin 4 agonist: DV, drug development
serotonin 4 agonist: DO, drug dose
serotonin 4 agonist: PK, pharmacokinetics
serotonin 4 agonist: PD, pharmacology
serotonin 4 agonist: PO, oral drug administration
serotonin 4 receptor: EC, endogenous compound
metoclopramide: AE, adverse drug reaction
metoclopramide: AN, drug analysis
metoclopramide: CM, drug comparison
metoclopramide: PD, pharmacology
bemesetron: AN, drug analysis
bemesetron: CM, drug comparison
bemesetron: PD, pharmacology
tropisetron: AN, drug analysis
tropisetron: CM, drug comparison
tropisetron: PD, pharmacology
renzapride: AE, adverse drug reaction
renzapride: AN, drug analysis
renzapride: CM, drug comparison
renzapride: PD, pharmacology
zacopride: AN, drug analysis
zacopride: CM, drug comparison
zacopride: PD, pharmacology
cisapride: AE, adverse drug reaction
cisapride: AN, drug analysis
cisapride: PD, pharmacology
ondansetron: AN, drug analysis
ondansetron: CM, drug comparison
ondansetron: PD, pharmacology
3 ethyl 2,3 dihydro 2 oxo 1 benzimidazolecarboxylic acid 3alpha tropanylamide: AN, drug analysis
3 ethyl 2,3 dihydro 2 oxo 1 benzimidazolecarboxylic acid 3alpha tropanylamide: PD, pharmacology
2,3 dihydro 3 isopropyl 2 oxo 1 benzimidazolecarboxylic acid 3alpha tropanylamide: AN, drug analysis
2,3 dihydro 3 isopropyl 2 oxo 1 benzimidazolecarboxylic acid 3alpha tropanylamide: PD, pharmacology
itasetron: AN, drug analysis
itasetron: PD, pharmacology
8 amino 7 chloro 1,4 benzodioxan 5 carboxylic acid 1 butyl 4 piperidinylmethyl ester: AN, drug analysis
8 amino 7 chloro 1,4 benzodioxan 5 carboxylic acid 1 butyl 4 piperidinylmethyl ester: DV, drug development
8 amino 7 chloro 1,4 benzodioxan 5 carboxylic acid 1 butyl 4 piperidinylmethyl ester: DO, drug dose
8 amino 7 chloro 1,4 benzodioxan 5 carboxylic acid 1 butyl 4 piperidinylmethyl ester: PD, pharmacology
8 amino 7 chloro 1,4 benzodioxan 5 carboxylic acid 1 butyl 4 piperidinylmethyl ester: PO, oral drug administration
clebopride: AN, drug analysis
clebopride: PD, pharmacology
1 (4 amino 5 chloro 2 methoxyphenyl) 3 (1 butyl 4 piperidinyl) 1 propanone: AN, drug analysis
1 (4 amino 5 chloro 2 methoxyphenyl) 3 (1 butyl 4 piperidinyl) 1 propanone: DV, drug development
1 (4 amino 5 chloro 2 methoxyphenyl) 3 (1 butyl 4 piperidinyl) 1 propanone: PK, pharmacokinetics
1 (4 amino 5 chloro 2 methoxyphenyl) 3 (1 butyl 4 piperidinyl) 1 propanone: PD, pharmacology

4 amino 5 chloro n (octahydro 6 methyl 2h quinolizin 2 yl) ortho anisamide: AN, drug analysis
4 amino 5 chloro n (octahydro 6 methyl 2h quinolizin 2 yl) ortho anisamide: PD, pharmacology
1 methyl 3 indolecarboxylic acid [1 [2 (methylsulfonylamino)ethyl] 4 piperidinylmethyl] ester: AN, drug analysis
1 methyl 3 indolecarboxylic acid [1 [2 (methylsulfonylamino)ethyl] 4 piperidinylmethyl] ester: DV, drug development
1 methyl 3 indolecarboxylic acid [1 [2 (methylsulfonylamino)ethyl] 4 piperidinylmethyl] ester: PK, pharmacokinetics
1 methyl 3 indolecarboxylic acid [1 [2 (methylsulfonylamino)ethyl] 4 piperidinylmethyl] ester: PD, pharmacology
serotonin 3 antagonist: AN, drug analysis
serotonin 3 antagonist: CM, drug comparison
serotonin 3 antagonist: PD, pharmacology
4 amino 5 chloro n [(hexahydro 1h pyrrolizin 1 yl)methyl] 2 methoxybenzamide: AN, drug analysis
4 amino 5 chloro n [(hexahydro 1h pyrrolizin 1 yl)methyl] 2 methoxybenzamide: CM, drug comparison
4 amino 5 chloro n [(hexahydro 1h pyrrolizin 1 yl)methyl] 2 methoxybenzamide: DV, drug development
4 amino 5 chloro n [(hexahydro 1h pyrrolizin 1 yl)methyl] 2 methoxybenzamide: PD, pharmacology
tegaserod: AN, drug analysis
tegaserod: PD, pharmacology
piboserod: AN, drug analysis
piboserod: DV, drug development
piboserod: PD, pharmacology
piboserod: PO, oral drug administration
4 amino 5 chloro 2,3 dihydro 2 methyl n [2 (8 pyrrolizidinyl)ethyl]benzo[b]furan 7 carboxamide: AN, drug analysis
4 amino 5 chloro 2,3 dihydro 2 methyl n [2 (8 pyrrolizidinyl)ethyl]benzo[b]furan 7 carboxamide: CM, drug comparison
4 amino 5 chloro 2,3 dihydro 2 methyl n [2 (8 pyrrolizidinyl)ethyl]benzo[b]furan 7 carboxamide: PD, pharmacology
1 (4 amino 5 chloro 2 methoxyphenyl) 3 [1 [2 (methanesulfonamido)ethyl] 4 piperidinyl] 1 propanone: AN, drug analysis
1 (4 amino 5 chloro 2 methoxyphenyl) 3 [1 [2 (methanesulfonamido)ethyl] 4 piperidinyl] 1 propanone: PD, pharmacology
prucalopride: AN, drug analysis
prucalopride: PD, pharmacology
mosapride citrate: AN, drug analysis
mosapride citrate: PD, pharmacology
4 amino 5 chloro 2 methoxybenzoic acid 3 piperidinopropyl ester: AN, drug analysis
4 amino 5 chloro 2 methoxybenzoic acid 3 piperidinopropyl ester: PD, pharmacology
4 amino 5 chloro 2 methoxybenzoic acid 2 (diethylamino)ethyl ester: AN, drug analysis
4 amino 5 chloro 2 methoxybenzoic acid 2 (diethylamino)ethyl ester: PD, pharmacology

benzoic acid derivative: AN, drug analysis
benzoic acid derivative: PD, pharmacology
unindexed drug
sb 207058
ts 951 k
ml 1035
brl 24682
sc 52246
6 chloro n [(hexahydro 1h pyrrolizin 1 yl)methyl]imidazo[1,2 a]pyridine 8 carboxamide
4 amino 5 chloro n [2 (1 dimethylamino 1 cyclohexyl)ethyl] 2 methoxybenzamide
sc 52491
y 34959
4 amino 5 chloro 2 methoxybenzoic acid 2 (1 piperidinyl)ethyl ester
4 amino 5 chloro 2 methoxybenzoic acid 2 (3,5 dimethylpiperidino)ethyl ester
2 chloro 5 methoxy 4 [5 (2 piperidylmethyl) 1,2,4 oxadiazol 3 yl]aniline
sb 205800
8 amino 7 iodo 1,4 benzodioxan 5 carboxylic acid 1 butyl 4 piperidinylmethyl ester
rs 17017
rs 67532
rs 39604
rs 100302
rs 100235
3 indolecarboxylic acid 2 (1 piperidinyl)ethyl ester
gr 124487
sb 204139
n [2 [4 (1 adamantanecarboxamido) 1 piperidinyl]ethyl] 1 isopropyl 1h indazole 3 carboxamide
2,3 dihydro 2 oxo 1 benzimidazolecarboxylic acid 6 methoxy 3alpha tropanyl ester
ts 951
4 amino 5 chloro n (1 ethyl 2 hydroxymethyl 4 pyrrolidinyl) 2 methoxybenzamide
5 fluoro 2 methoxy 1h indole 3 carboxylic acid 1 [2 (methylsulfonamido)ethyl] 4 piperidinylmethyl ester

CAS REGISTRY NO.: (metoclopramide) 12707-59-4, 2576-84-3, 364-62-5, 7232-21-5; (bemesetron) 40796-97-2; (tropisetron) 89565-68-4; (renzapride) 109872-41-5; (zacopride) 90182-92-6, 99617-34-2; (cisapride) 81098-60-4; (ondansetron) 103639-04-9, 116002-70-1, 99614-01-4; (3 ethyl 2,3 dihydro 2 oxo 1 benzimidazolecarboxylic acid 3alpha tropanylamide) 127595-43-1; (2,3 dihydro 3 isopropyl 2 oxo 1 benzimidazolecarboxylic acid 3alpha tropanylamide) 134296-40-5; (itasetron) 127618-28-4; (8 amino 7 chloro 1,4 benzodioxan 5 carboxylic acid 1 butyl 4 piperidinylmethyl ester) 148702-58-3; (clebopride) 55905-53-8; (1 (4 amino 5 chloro 2 methoxyphenyl) 3 (1 butyl 4 piperidinyl) 1 propanone) 168986-60-5; (4 amino 5 chloro n (octahydro 6 methyl 2h quinolizin 2 yl) ortho anisamide) 99390-76-8; (1 methyl 3 indolecarboxylic acid [1 [2 (methylsulfonylamino)ethyl] 4 piperidinylmethyl] ester) 144625-51-4; (4 amino 5 chloro n [(hexahydro 1h pyrrolizin 1 yl)methyl] 2 methoxybenzamide) 141196-99-8; (tegaserod) 145158-71-0, 189188-57-6; (piboserod) 152811-62-6, 178273-87-5; (4 amino 5 chloro 2,3 dihydro 2 methyl n [2 (8

pyrrolizidinyl)ethyl]benzo[b]furan 7 carboxamide) 166743-12-0; (1 (4 amino 5 chloro 2 methoxyphenyl) 3 [1 [2 (methanesulfonamido)ethyl] 4 piperidinyl] 1 propanone) 168986-61-6; (prucalopride) 179474-80-7, 179474-81-8, 179474-84-1; (mosapride citrate) 112885-42-4; (4 amino 5 chloro 2 methoxybenzoic acid 3 piperidinopropyl ester) 149719-06-2; (8 amino 7 iodo 1,4 benzodioxan 5 carboxylic acid 1 butyl 4 piperidinylmethyl ester) 148703-08-6; (3 indolecarboxylic acid 2 (1 piperidinyl)ethyl ester) 135938-17-9; (2,3 dihydro 2 oxo 1 benzimidazolecarboxylic acid 6 methoxy 3alpha tropanyl ester) 123258-98-0; (5 fluoro 2 methoxy 1h indole 3 carboxylic acid 1 [2 (methylsulfonamido)ethyl] 4 piperidinylmethyl ester) 144625-67-2

CHEMICAL NAME: (1) Sb 204070; (2) Sb 207058; (3) Sb 207266; Ym 53389; Sb 205800; Sb 207710; Rs 17017; Gr 113808; Rs 67333; Rs 67506; Rs 67532; Rs 39604; Rs 100302; Sb 203186; Rs 100235; Gr 124487; Sb 204139; Ly 353433; Sdz htf 919; Dau 6285; Ts 951; ***Tks 159***; Gr 125487d; Rs 23597 190; Ml 10375; Mdl 72222; Ics 205930; Brl 24924; Bimu 1; Bimu 8; Dau 6215; Ts 951 k; Ml 1035; Brl 20627; Brl 24682; Sc 53116; Sc 52246; Sc 53606; Sk 951; Ym 47813; Sc 52491; Y 34959; Sdz 205557; Ml 10302; Rs 23597

COMPANY NAME: (3) SmithKline Beecham

L86 ANSWER 18 OF 22 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1999377316 EMBASE

TITLE: ***Gastroduodenal motility.***

AUTHOR: Quigley E.M.M.

CORPORATE SOURCE: Dr. E.M.M. Quigley, Department of Medicine, Clinical Sciences Building, Cork University Hospital, Cork, Ireland. equigley@ucc.ie

SOURCE: Current Opinion in Gastroenterology, (1999) Vol. 15, No. 6, pp. 481-491. .
Refs: 172
ISSN: 0267-1379 CODEN: COGAEK

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 006 Internal Medicine
037 Drug Literature Index
048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 18 Nov 1999
Last Updated on STN: 18 Nov 1999

ABSTRACT: Several major themes emerged over the past year in the area of ***gastroduodenal*** ***motility.*** Mostly, these themes represented extensions of research areas discussed in prior reviews in this series rather than the emergence of completely new concepts. Thus, for example, considerable emphasis has again been placed on regional ***gastric*** motor function in dyspepsia and on the role of fundic relaxation and accommodation, in particular. Not surprisingly, basic physiologic research has also shown a keen interest in the regulation of fundic relaxation. One new and exciting development is the recognition of the ***stomach***'s role in satiety. The spectrum of ***gastric*** motor dysfunction in diabetes mellitus continues to be explored, and the important role of hyperglycemia in regulating ***gastric*** function has been further emphasized. More data have been provided on noninvasive alternatives to ***gastric*** motor function testing, and several studies have looked at factors that may influence

variability in these various tests. There have been few innovations over the past year in the therapeutic arena; rather, the indications and limitations of current therapies have been further developed.

CONTROLLED TERM: Medical Descriptors:
gastrointestinal motility
dyspepsia: DI, diagnosis
dyspepsia: DT, drug therapy
satiety
hyperglycemia: DI, diagnosis
stomach motility
stomach paresis: DI, diagnosis
stomach paresis: ET, etiology
percutaneous endoscopic gastrostomy
acupuncture
human
article
Drug Descriptors:
*histamine h2 receptor antagonist: DT, drug therapy
*histamine h2 receptor antagonist: PD, pharmacology
*domperidone: DT, drug therapy
*domperidone: PD, pharmacology
serotonin 4 agonist: DV, drug development
serotonin 4 agonist: PD, pharmacology
tks 159: DV, drug development
tks 159: PD, pharmacology
glucagon like peptide 1: EC, endogenous compound
erythromycin: DT, drug therapy
erythromycin: PD, pharmacology
CAS REGISTRY NO.: (domperidone) 57808-66-9; (glucagon like peptide 1) 89750-14-1; (erythromycin) 114-07-8, 70536-18-4
CHEMICAL NAME: ***Tks 159***

L86 ANSWER 19 OF 22 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1995:247381 BIOSIS
DOCUMENT NUMBER: PREV199598261681
TITLE: Effect of ***TKS159***, a novel 5-hydroxytryptamine 4 agonist, on gastrointestinal contractile activity in conscious dogs.
AUTHOR(S): Haga, N.; Shiba, Y.; Mochiki, E.; Itoh, Z.
CORPORATE SOURCE: GI Res. Labs., Inst. Molecular and Cellular Regulation, Gunma Univ., Maebashi, Japan
SOURCE: Gastroenterology, (1995) Vol. 108, No. 4 SUPPL., pp. A609. Meeting Info.: 95th Annual Meeting of the American Gastroenterological Association and Digestive Disease Week. San Diego, California, USA. May 14-17, 1995. CODEN: GASTAB. ISSN: 0016-5085.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Jun 1995
Last Updated on STN: 11 Jul 1995
CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Biochemistry methods - Proteins, peptides and amino acids 10054
Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064

Anatomy and Histology - Experimental anatomy 11104
Anatomy and Histology - Surgery 11105
Anatomy and Histology - Regeneration and transplantation 11107
Movement 12100
Pathology - Therapy 12512
Metabolism - Proteins, peptides and amino acids 13012
Digestive system - Physiology and biochemistry 14004
Digestive system - Pathology 14006
Nervous system - Anatomy 20502
Nervous system - Physiology and biochemistry 20504
Pharmacology - Drug metabolism and metabolic stimulators 22003
Pharmacology - Clinical pharmacology 22005
Pharmacology - Digestive system 22014

INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Digestive System (Ingestion and Assimilation); Metabolism; Morphology; Nervous System (Neural Coordination); Pharmacology; Physiology; Surgery (Medical Sciences)

INDEX TERMS: Chemicals & Biochemicals
5-HYDROXYTRYPTAMINE; ACETYLCHOLINE

INDEX TERMS: Miscellaneous Descriptors
ENDOGENOUS ACETYLCHOLINE RELEASE; GASTROINTESTINAL-DRUG; GASTROKINETIC AGENT; MEETING ABSTRACT; PHARMACODYNAMICS; ***TKS159***; VAGAL DENERVATION; VAGOTOMY-ASSOCIATED DYSMOTILITY

ORGANISM: Classifier
Canidae 85765
Super Taxa
Carnivora; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
Canidae
Taxa Notes
Animals, Carnivores, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates

REGISTRY NUMBER: 50-67-9 (5-HYDROXYTRYPTAMINE)
51-84-3 (ACETYLCHOLINE)

L86 ANSWER 20 OF 22 USPATFULL on STN
ACCESSION NUMBER: 2005:324995 USPATFULL
TITLE: Non nucleoside reverse transcriptase inhibitors
INVENTOR(S): Deroy, Patrick, Laval, CANADA
Faucher, Anne-Marie, St-Placide, CANADA
Gagnon, Alexandre, Montreal, CANADA
Landry, Serge, St-Jerome, CANADA
Morin, Sebastien, Montreal, CANADA
O'Meara, Jeffrey, Boisbriand, CANADA
Simoneau, Bruno, Laval, CANADA
Thavonekham, Bounkham, Longueuil, CANADA
Yoakim, Christiane, Laval, CANADA
PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Ingelheim, GERMANY, FEDERAL REPUBLIC OF (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005282907	A1	20051222

APPLICATION INFO.: US 2005-137831 A1 20050524 (11)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2004-575888P	20040601 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MICHAEL P. MORRIS, BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY RD, P O BOX 368, RIDGEFIELD, CT, 06877-0368, US
NUMBER OF CLAIMS: 34
EXEMPLARY CLAIM: 1
LINE COUNT: 5025
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds of formula (I): ##STR1## wherein Ar, X, R.sup.1, R.sup.2, R.sup.3 and R.sup.4 are as defined herein. The compounds are useful as reverse transcriptase inhibitors against wild type and single or double mutant strains of HIV.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT

871473-74-4P	871473-75-5P	871473-76-6P	871473-77-7P	871473-78-8P
871473-79-9P	871473-80-2P	871473-81-3P	871473-82-4P	871473-83-5P
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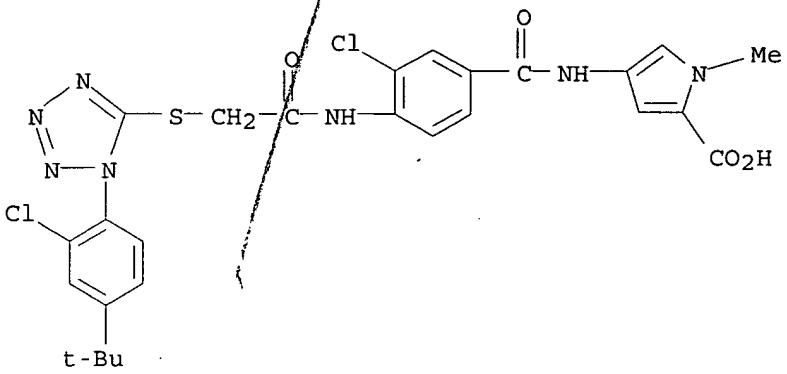
871476-23-2P 871476-24-3P 871476-25-4P 871476-26-5P
(drug candidate; preparation of acetamide derivs. as reverse transcriptase inhibitors for treatment of HIV infection)

IT ***871475-96-6P***
(drug candidate; preparation of acetamide derivs. as reverse transcriptase inhibitors for treatment of HIV infection)

RN 871475-96-6 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 4-[[3-chloro-4-[[[[1-[2-chloro-4-(1,1-dimethylethyl)phenyl]-1H-tetrazol-5-yl]thio]acetyl]amino]benzoyl]amino]-1-methyl- (9CI) (CA INDEX NAME)



L86 ANSWER 21 OF 22 USPATFULL on STN

ACCESSION NUMBER: 2002:308379 USPATFULL

TITLE: Medicament

INVENTOR(S): Skogvall, Staffan, Lund, SWEDEN

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002173505	A1	20021121
APPLICATION INFO.:	US 2001-984329	A1	20011029 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	SE 1999-1531	19990428
	SE 1999-1906	19990526
	SE 1999-2251	19990615
	SE 1999-2252	19990615
	WO 2000-SE819	20000428
	US 1999-131355P	19990428 (60)
	US 1999-136604P	19990527 (60)
	US 1999-139632P	19990617 (60)
	US 1999-139633P	19990617 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: SMITH, GAMBRELL & RUSSELL, LLP, ATTORNEYS AT LAW, SUITE 800, 1850 M STREET, N.W., WASHINGTON, DC, 20036

NUMBER OF CLAIMS: 14

EXEMPLARY CLAIM: 1
LINE COUNT: 567
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A compound having agonist activity to the ***5-HT***.sub.4 receptor for use as a medicament and the use of said compound in the manufacture of a medicament for use in therapeutic or prophylactic treatment of disorders involving bronchocontraction of a human or animal body is described, as well as methods of treatment, wherein said compounds are administered. Further, a compound having antagonist activity to the ***5-HT***.sub.2a receptor for use as a medicament and the use of said compound in the manufacture of a medicament for use in therapeutic or prophylactic treatment or disorders involving bronchocontraction of a human or animal body is described, as well as methods of treatment, wherein said compounds are administered. Moreover, a composition comprising a combination of compounds comprising at least one compound with agonist activity to the ***5-HT***.sub.4 receptor agonist and at least one compound with antagonist activity to the ***5-HT***.sub.2, receptor antagonist is described, as well as such a composition for use as a medicament, the use of said composition for the manufacture of a medicament for therapeutic or prophylactic treatment of disorders involving broncocontraction of a human or animal body, and methods of treatment, wherein said compositions are administered.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A compound having agonist activity to the ***5-HT***.sub.4 receptor for use as a medicament and the use of said compound in the manufacture of a medicament for use. . . . described, as well as methods of treatment, wherein said compounds are administered. Further, a compound having antagonist activity to the ***5-HT*** .sub.2a receptor for use as a medicament and the use of said compound in the manufacture of a medicament for use. . . . are administered. Moreover, a composition comprising a combination of compounds comprising at least one compound with agonist activity to the ***5-HT***.sub.4 receptor agonist and at least one compound with antagonist activity to the ***5-HT***.sub.2, receptor antagonist is described, as well as such a composition for use as a medicament, the use of said composition. . . .

SUMM [0002] The present invention relates to a compound having agonist activity to the ***5-HT***.sub.4 receptor for use as a medicament and to the use of said compound in the manufacture of a medicament for. . .

SUMM [0003] Receptors of the ***5-HT*** (***serotonin***; 3-(P-aminoethyl)-5-hydroxyindole) type are well known and occur throughout the body, e.g. in the airways, and their relevance has mainly been reported in conjunction with treatment of CNS, muscle and ***gastric*** disorders, as disclosed in e.g. WO 98/18458 and U.S. Pat. No. 5,246,935. In such treatments, compounds having agonist activity to a ***5-HT***.sub.1 type receptor are often used. As examples of other 5-NT receptors, mention can be made of receptors of the ***5-HT***.sub.2, ***5-HT*** .sub.4, ***5-HT***.sub.5, ***5-HT6*** and ***5-HT***.sub.7 type. For a recent review of ***5-HT*** receptors, see Gerhardt, C. C. van Heerikhuizen, H., Eur. J. Phar., 334, 1-23 (1997), which is incorporated herein by reference.

SUMM [0004] Receptors of the ***5-HT***.sub.2 type are also well known, e.g. through U.S. Pat. Nos. 5,869,497, 5,705,519 and 5 246 935. The relevance of receptors of the ***5-HT***.sub.2 type has been reported in conjunction with e.g. CNS and neuronal disorders. Such disorders are often treated with compounds having

antagonist activity to a receptor of the .sup.*5-HT* .sub.2a, *5-HT*.sub.2B or *5-HT* .sub.2c type. Examples of such compounds are ritanserin and naftidroturyl. A review of typical agonists and antagonists of various *5-HT* receptors is disclosed in R. A. Glennon, Neuroscience and Biobehavioral Reviews, 14, 35-47 (1990), the whole content of which is. . .

SUMM [0005] SU 1 701 320 A1 discloses the use of ***serotonin*** for treatment of acute asthma attacks. This reference does not suggest any receptor mechanism for ***serotonin***, which is a compound with both a contracting and a relaxing effect on the airways, as is further discussed herein. . .

SUMM [0007] The present invention is based on the novel finding that certain *5-HT* receptors are of utmost importance in regulating bronchocontraction. In summary, it is disclosed herein that compounds having agonist activity to the *5-HT*.sub.4 receptor bring about a bronchorelaxing action upon administration thereof, and are therefore suitable as agents for treatment of bronchocontraction disorders. It is also disclosed herein that compounds having antagonist activity to the *5-HT*.sub.2, especially *5-HT*.sub.2a, receptor, are suitable agents in the treatment of bronchocontraction disorders. Methods for treatment of bronchocontraction disorders are also disclosed.

SUMM [0009] Accordingly, the present invention relates, in one of its aspects, to a compound having agonist activity to the *5-HT*.sub.4 receptor for use as a medicament. In another aspect it relates to use of said compound in the manufacture of. . .

SUMM [0010] In a preferred embodiment, the invention relates to the use of a compound having agonist activity to the *5-HT*.sub.4 receptor in the manufacture of a medicament for therapeutic or prophylactic treatment of disorders involving bronchocontraction, wherein said agonist has. . .

SUMM [0012] In a preferred embodiment, the invention relates to the use of a compound having antagonist activity to a *5-HT*.sub.2, receptor in the manufacture of a medicament for therapeutic or prophylactic treatment of disorders involving bronchocontraction, wherein said antagonist has. . .

SUMM [0014] The present invention also relates to the use of a compound having antagonist activity to a *5-HT*.sub.2a receptor in combination with a compound having agonist activity to the *5-HT*.sub.4 receptor in the manufacture of a medicament for therapeutic or prophylactic treatment of disorders involving bronchocontraction. In a preferred embodiment said compound having agonist activity is ***serotonin*** or a derivative thereof having agonist activity to the *5-HT*.sub.4 receptor. This combination of the *5-HT2a* receptor antagonist and the agonist increases the ***serotonin*** transmission in the body, particularly in the presence of a ***serotonin*** uptake inhibitor (SRI) - Further, the compounds having agonist activity to the *5-HT*.sub.4 receptor to be used according to the present invention are also useful in the present combination embodiment. In particular, said. . .

SUMM [0015] According to the present invention several known substances are, surprisingly, able to stimulate the *5-HT*.sub.4 receptor, without activating the contracting *5-HT* .sub.2a receptor, thereby generating a relaxing effect on the bronchocontraction. Such agonist compounds are selected from the group comprising the substances. . .

SUMM [0023] According to the present invention several known antagonist compounds are, surprisingly, able to influence the *5-*

HT2a receptor, thereby generating a contraction reducing effect, i.e. a relaxation effect, and are selected from a group comprising ketanserin, AMI-193. . .

SUMM . . . NE-100, Nefazodone, N-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline, NRA0045, Olanzapine, Ondansetron, 1-(2-pyritnidinyl)piperazine derivatives, Pizotifen, raclopride, Roxindole, Risperidone, Ritanserin, RP62203, sarpogrelate and its active metabolite (M-1), ***serotonin*** reuptake inhibitors like fluoxetine, YM 992, medifoxamine, ericlamine, imipramine, iprindole, BIMT 17, citalopram, paroxetine, sertraline, fluvoxamine spiro indoles N-substituted with. .

SUMM [0027] Ketanserin is excluded from the embodiment concerning the ***5-HT***.sub.2 receptor antagonist compound for use as a medicament.

SUMM . . . or animal patient a therapeutically effective amount of a compound according to the present invention having antagonist activity to a ***5-HT***.sub.2a receptor. Preferably, said method relates to treatment of asthma and disorders related thereto.

SUMM . . . the contraction in the airways caused (1) either by the underlying disease (asthma etc) or (2) by the administration of ***5-HT*** or other substances with ***5-HT*** .sub.2a-activating properties. The level of contraction in the airways can, for instance, be determined by spirometric measurements of the Forced Expiratory. . .

SUMM . . . As appears from FIG. 1, the contractile component often manifests itself as a reduction or a complete elimination of the ***5-HT*** induced relaxation, rather than in an increase of force from the control (pre-exposure) level. In the case of "specific" agonists to the ***5-HT***.sub.4 receptor, this sustained relaxing effect is achieved because the contractile ***5-HT2a*** receptor is not affected; only the relaxing ***5-HT***.sub.4 receptor is activated. In the case of antagonists to the ***5-HT***.sub.2a receptor, this effect is achieved due to direct blocking of the ***5-HT***.sub.2-, receptor, whereby the unspecific agonists to the ***5-HT***.sub.4 receptor, such as ***5-HT***, can act without also causing contraction by the ***5-HT***.sub.2, receptor.

SUMM . . . embodiment may optionally include two or more of the above outlined compounds, Furtherr in the embodiment when the compound having ***5-HT***.sub.2, antagonist activity is administered, optionally together with complementary ***serotonin*** or derivatives thereof, a ***serotonin*** uptake inhibitor can be added with a view to amplifying the relaxing effect.

SUMM [0035] Said medicament may be prepared as a composition adapted either for administration via the respiratory ***tract*** or for oral, intravenous, topical, intraperitoneal or subcutaneous administration, in association with one or more pharmaceutically acceptable carriers, diluents or. . .

SUMM [0036] Moreover, said medicament is preferably administered via the respiratory ***tract*** in the form of e.g. an aerosol or an air-suspended fine powder. However, in some cases a useful alternative to administration via the respiratory ***tract*** may be oral, topical, parenteral, subcutaneous, transdermal or rectal administration, wherein e.g. tablets, capsules, powders, microparticles, granules, syr-ups, suspensions,. . .

SUMM [0037] FIG. 1 depicts the effects of ***5-HT*** and selective ***5-HT***.sub.4 agonists on the spontaneous tone in human in vitro preparations. Note that ***5-HT*** only gives a transient relaxation, while selective ***5-HT***.sub.4 agonists give a strong sustained relaxing effect.

DETD [0040] Later experiments, not included in the thesis, have revealed that one of the regulating factors is ***serotonin***, also called ***5-HT***, which exerts agonist action on the receptors ceptors ***5-HT***.sub.4, ***5HT***.sub.5, ***5-HT***.sub.6, ***5-HT***.sub.7 as well as on ***5-HT***.sub.2 receptors.

DETD [0041] Additional experiments have shown that when 1 μM ***serotonin*** was added to denuded airway smooth muscle preparations from the guinea-pig displaying a strong, smooth spontaneous tone, the average force level was increased significantly, i.e. a contraction was observed. A contractile effect of ***serotonin*** on airway smooth muscle has been reported in e.g. SkQgvall, S., Korsgren, M-, Grampp, W., J. Appl. Phys., 86:789-798, 1999. However, when 10 μM of ***serotonin*** was added, the spontaneous tone was significantly suppressed to a level of about half the force observed in control (drug-free). . . its normal level when the preparations were again exposed to control conditions. Thus, it has now surprisingly been shown that ***serotonin*** brings about contraction of the airways at low concentrations and relaxation at high concentrations, consequently having a dual effect on. . .

DETD [0042] Furthermore, it has been shown that when the contracting ***5-HT2***, receptor was blocked with ketanserin, the S-ST, i.e. ***serotonin***, induced almost no contraction, but instead only a significant relaxation. Similar experiments have also been performed on human in vitro preparations, from patients undergoing lobecotomy or pulmectomy due to lung cancer. It was found that in this tissue, ***5-HT*** was even more potent in relaxing the airway smooth muscle than in guinea pig. In human tissue, already 1 μM ***5-HT*** induces a significant relaxation of the spontaneous tone.

DETD . . . a weak contraction when exposed to S-HT. Nevertheless, examinations on spontaneous tone on human in vitro preparations have shown that ***5-HT*** indeed has a contractile component also in this tissue. However, this contraction takes a longer time to develop than in. . . 1). The transient nature of the 5-ET relaxation is most likely caused by a simultaneous activation of the fast, relaxing ***5-HT***.sub.4 receptor, and a slower activation of the contracting SHT.sub.2a receptor. This is clear, because activation of the relaxing ***5-HT***.sub.4 receptor by a Substance that lacks ***5-HT***.sub.2, receptor activating properties (such as 5-carboxiamidotryptamine or SC 53116), results in a relaxation that is persistent and not transient (see. . .

DETD . . . be useful in the treatment of bronchoobstructive diseases. In SU 1 701 320 it is suggested that the 5-Hr.sub.1 i.e. ***serotonin*** , may be of use as an addition to standard beta2 receptor stimulation. However, from our experiments it seems clear that. . . asthmatic disorders, because of the transient relaxing effect by S-HrT (see FIG. 1). If instead, as we propose herein, a ***5-HT*** analogue that lacks the ***5-HT2a*** activating properties is given, the relaxing effect is persistent, and not transient.

DETD [0045] In summary, it has now been discovered that agonist action on the ***5-HT***.sub.4 receptor results in a relaxing effect, whereas agonist action on ***5-HT2a*** receptors results in a contractile effect. In conclusion, the dual effect of ***serotonin*** is most likely a result of its agonist action on the relaxing 5-UT.sub.4 receptor as well as on the contracting ***5-HT***.sub.27 receptor.

DETD [0046] It was also deduced from these experiments that compounds having agonist activity to the ***5-HT***.sub.4 receptor, while having only low or no agonist activity to a ***5-HT***

.sub.2a receptor, therefore are useful as agents for treatment of bronchocontraction disorders.

DETD [0047] Thus, the present invention relates to the use of compounds having agonist activity to the ***5-HT***.sub.4 receptor in the manufacture of a medicament intended for treatment of bronchocontraction disorders, whereby said compounds have the strong bronchorelaxing effect of ***serotonin*** but have substantially no contractile effect. As mentioned above, the compounds used according to the present invention have only low or no agonist activity to ***5-HT***.sub.2a receptors.

DETD [0048] In the above mentioned experiments it has also been shown that compounds having antagonist activity to a ***5-HT2***. receptor are useful as agents for treatment of bronchocontraction disorders, since they are capable of blocking the contractile effect of a compound having agonist activity to a ***5-HT***.sub.2, receptor. The compounds according to the present invention having antagonist activity to the ***5-HT***.sub.2, receptor may even be administered together with ***serotonin*** in the form of a complement so the ***serotonin*** content already present in the body with a view to obtaining an amplified contracting effect, or with any other substance having agonist activity to the ***5-HT2a*** receptor; or with a ***serotonin*** uptake inhibitor Said administration can be simultaneous or sequential, and a powerful relaxing effect on the bronchi can be achieved. . . this manner. Thus, the present invention also relates to the combined use of a compound having antagonist activity to a ***5-HT2*** ,-receptor and a compound having agonist activity to the ***5-HT***.sub.4 receptor, in the manufacture of a medicament for therapeutic or prophylactic treatment of disorders involving bronchocontraction.

CLM What is claimed is:

1. Use of one or more compounds having antagonist activity to a ***5-HTI***. receptor, and derivatives and pharmaceutically acceptable salts thereof having antagonist activity to the ***5-HT***.sub.2. receptor in the manufacture of a medicament for therapeutic or prophylactic treatment of disorders involving human bronchocontraction chosen from the. . .

. . Nefazodone, N-ethoxycarbonyl-2-ethoxy-i,2-dihydroquinoline, NRA0045, olanzapine, Ondansetron, 1-(2-pyrimidinyl) piperazine derivatives, Pizotifen, raclopride, Roxindole, Risperidone, Ritanserin, RP62203, sarpogrelate and its active metabolite (M-1), ***serotonin*** reuptake inhibitors like fluoxetine, YM 992, meditoxamine, ericlamine, imipramine, iprindole, BIMT 17, citalopram, paroxetine, sertraline, fluvoxamine Spiro indoles N-substituted with. . .

6. Use of one or more compounds having agonist activity to a ***5-HT***.sub.4 receptor in the manufacture of a medicament for therapeutic or prophylactic treatment of disorders involving human bronchocontraction, chosen from the. . .

10. Use of a composition comprising a combination of at least one compound with agonist activity to the ***5-HT***-.sub.4 receptor, and at least one compound with antagonist activity to the ***5-HT2a*** receptor for the manufacture of a medicament for therapeutic or prophylactic treatment of disorders involving bronchocontraction, chosen from the group. . .

. . least 60%, and most preferably at least 90%, and wherein said combination is chosen from the following groups of a) ***5-HT***.sub.4 receptor agonists, and b) ***5-HT*** .sub.2. receptor antagonists, or derivatives or pharmaceutically acceptable salts thereof: a) ***5-HT***.sub.4 receptor agonists: 5-carboxamidotryptamine, lIMU 1, BIMU 8, BRL 24924, Cisapride,

DAU 6236, 5-hydroxy-N,N-dimetyltryptamin, ML-1035, ML 10302, 5-metoxytryptamin, Metoclopramide, Mosapride, 8-OH-DPAT. . . 216-454, SR59768, TKS159, VB20B7, YM-4781,3, YM-53389, S YM-09151, Zacopride, Zelmac, arylcarbamate derivatives of I-piperidineethanol, 2-piperazinylbenzoxazole derivatives, clebopride, and ##STR10## and ***serotonin*** (***5-HT***) and derivatives and pharmaceutically acceptable salts thereof. b) S-HT.sub.2a receptor antagonists: AMI-193 and MDL 100,907, ALEPH-2, Amperozide, amesergide, aryloxyalkylimidazolines, 1-aryl-4-propylpiperazines,. . . Nefazodone, N-ethoxycarbonyl-2-ethoxy-1,2-diydroquinoline, NRA0045, Olanzapine, Ondansetron, 1-(2-pyrimidinyl) piperazine derivatives, Pizotifen, raclopride, Roxindole, Risperidone, Ritanserin, RP62203, sarpogrelate and its active metabolite (M-1), ***serotonin*** reuptake inhibitors like fluoxetine, YM 992, medifoxamine, ericlamine, imipramine, iprindole, BIMT 17, citalopram, paroxetine, sertraline, fluvoxamine spiro indoles N-substituted with. . .

12. Use according to claim 11, wherein the composition comprises the following combinations of a ***5-HT***,.sub.4 receptor agonist and a ***5-HT***.sub.2, receptor antagonist: VB20B7 and AMI-193, VB20B7 and MDL 11939, RS67333 and AMI-193, RS67333 and MDL 11939, VB20B7 and WAY 100635,. . .

. . . obstructive pulmonary disease, wherein said method comprises administering to a human or animal patient a therapeutically effective amount of a ***5-HT***.sub.4 receptor agonist according to any one of claims 6 and 7 and a ***5-HT***.sub.2a receptor antagonist according to any one of claims 1-3, either simultaneously or sequentially.

IT 50-37-3, LSD 50-49-7, Imipramine 50-67-9D, Serotonin, derivs. 110-85-0D, Piperazine, aryl derivs., biological studies 129-03-3, Cyproheptadine 361-37-5, Methysergide 364-62-5, Metoclopramide 487-93-4, 5-Hydroxy-N,N-dimethyltryptamine 510-74-7, AMI-193 548-43-6, Elymoclavine 608-07-1, 5-Methoxytryptamine 749-02-0, Spiperone 4205-90-7, Clonidine 5560-72-5, Iprindole 15574-96-6, Pizotifen 16357-59-8, N-Ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline 17692-51-2, Metergoline 20980-22-7D, 1-(2-Pyrimidinyl)piperazine, derivs. 24219-97-4, Mianserin 28299-33-4D, Imidazoline, aryloxyalkyl derivs. 32359-34-5, Medifoxamine 32896-53-0, LY 53857 free base 54739-18-3, Fluvoxamine 54910-89-3, Fluoxetine 59729-33-8, Citalopram 61869-08-7, Paroxetine 64795-35-3, Mesulergine 67537-81-9D, Hexahydrocarbazole, derivs. 74050-98-9, Ketanserin 74885-09-9, 5-Carboxamidotryptamine 75272-39-8, YM 09151 75558-90-6, Amperozide 78950-78-4, 8-OH-DPAT 79617-96-2, Sertraline 81098-60-4, Cisapride 83366-66-9, Nefazodone 84225-95-6, Raclopride 84625-59-2, Dotarizine 85273-96-7, ICI 169369 87051-43-2, Ritanserin 90182-92-6, Zacopride 99614-02-5, Ondansetron 99746-68-6, (R,R)-LY-53857 99746-70-0, (S,R)-LY-53857 99746-72-2, (R,S)-LY-53857 100746-36-9, CGS 18102A 100762-72-9, (S,S)-LY-53857 106266-06-2, Risperidone 107703-78-6, MDL 11939 109872-41-5, BRL 24924 112192-04-8, Roxindole 112727-80-7, Renzapride 112885-41-3, Mosapride 112922-55-1, Ericlamine 120444-71-5, Deramciclane 121588-75-8, Amesergide 122866-79-9, R 076186 125557-35-9 125926-17-2, Sarpogrelate 127266-56-2, WY 50324 127595-11-3, DAU 6236 127595-43-1, BIMU 1 127625-29-0, Fananserin 130580-02-8, SR 46349B 132539-06-1, Olanzapine 133364-63-3, DV 7028 134296-40-5, BIMU 8 136861-96-6, MDL 28133A 137328-52-0, LY 215840 138752-34-8, RS 56532 139290-65-6, MDL 100907 139290-69-0, MDL 100151 141196-99-8, SC-53116 ***142228-17-9***, TKS 159 146388-57-0, SC-49518 146714-97-8, WAY 100635 146714-97-8D, WAY 100635, derivs. 146715-07-3, Desmethyl-WAY 100635 148702-58-3, SB 204070 148868-55-7, ML 10302 149409-57-4 150527-23-4 150527-36-9, FG5893 hydrochloride

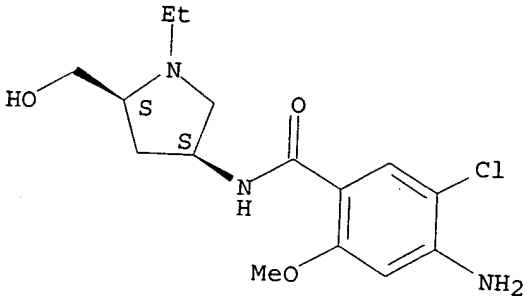
153415-44-2 155106-73-3, VB 20B7 161178-10-5, YM 992 161362-69-2, RS 67532 166743-12-0, SK-951 166815-18-5, RS 17017 167933-07-5, BIMT 17 168986-60-5, RS 67333 168986-61-6, RS 67506 169789-38-2, SDZ 216-454 172679-55-9, SR59768 175413-81-7, SB 205149 178485-02-4, ALEPH-2 179474-80-7, R 093877 179474-81-8, Prucalopride 183949-64-6, NRA0045 189188-57-6, Zelmac 193404-36-3, RS 57639 208661-17-0, LU 111995 217635-62-6 217635-64-8 220850-98-6, YM 53389 303953-05-1 303953-06-2 303955-07-9, YM 47813
(serotoninergic agonists and antagonists for treatment of bronchoconstriction-related disorders)

IT ***142228-17-9***, TKS 159
(serotoninergic agonists and antagonists for treatment of bronchoconstriction-related disorders)

RN 142228-17-9 USPATFULL

CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L86 ANSWER 22 OF 22 USPATFULL on STN

ACCESSION NUMBER: 92:72489 USPATFULL

TITLE: Benzamide derivatives

INVENTOR(S): Fujiwara, Hiromichi, Hyogo, Japan
Ogawa, Akihiko, Hyogo, Japan
Sakiyama, Hideyo, Hyogo, Japan
Tamura, Toshiaki, Hyogo, Japan

PATENT ASSIGNEE(S): Teikoku Chemical Industry Co., Ltd., Osaka, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5143935		19920901
APPLICATION INFO.:	US 1991-777011		19911016 (7)

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1990-277976	19901016

DOCUMENT TYPE: Utility

FILE SEGMENT: Granted

PRIMARY EXAMINER: Lee, Mary C.

ASSISTANT EXAMINER: McKane, Joseph K.

LEGAL REPRESENTATIVE: Wenderoth, Lind & Ponack

NUMBER OF CLAIMS: 5

EXEMPLARY CLAIM: 1

LINE COUNT: 723

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A benzamide derivative represented by the formula: ##STR1## having a

promoting activity of ***gastrointestinal tract*** and pharmacentical composition containing the same.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A benzamide derivative represented by the formula: ##STR1## having a promoting activity of ***gastrointestinal tract*** and pharmacentical composition containing the same.

SUMM The present invention relates to a class of novel benzamide derivatives each having a promoting activity to ***gastrointestinal tract***.

SUMM 4-Amino-5-chloro-N-((2-diethylamino) ethyl)-2-methoxy benzamide (common name: Metoclopramide) is a well-known compound having a promoting activity to ***gastrointestinal tract*** and especially to ***stomach***, and (±) 4-amino-5-chloro-N-(3R*,4S*)-1-(3-(p-fluorophenoxy)propyl)-3-methoxy-4-piperidyl)-o-anisamide (common name: Cisapride) is a well-known ***gastrokinetic*** compound customarily used for the treatment of chronic ***gastrics***, syndrome of ***gastrointestinal tract*** accompanied with ***postgastrectomy***, regurgitant esophagitis and suprious obstipation. Metoclopramide has, however, undesired properties of inducing exstrapyramidal syndrome and other undesired syndrome; due to. . .

SUMM Under the circumstances, it has long been desired to have a new medicinal compound which is excellent in absorption through ***gastrointestinal tract*** and has the least activity toward central nervous system.

SUMM . . . class of compounds having no or substantially no activity toward central nervous system and having an excellent promoting activity to ***digestive tract*** and especially to ***stomach***

.

SUMM Thus obtained compounds of the present invention are characterized in that they have excellent promoting activities to ***digestive tract*** and especially to ***stomach***, but no or substantially no activities toward central nervous system.

SUMM (1) Promoting activity to ***gastric*** emptying:

SUMM . . . 0.1 ml of aqueous 1.5% carboxymethyl cellulose solution containing 0.05% phenol red was orally administered. After leaving for 15 minutes, ***stomach*** was extracted and the phenol red amount remaining in the ***stomach*** was measured to determine the excreting activity for the tested compound.

DETD The present benzamide derivatives each has the properties for promoting activity to ***digestive tract*** and especially to ***stomach***.

DETD In mouse tests, ***stomach*** excretion promoting rates of the compounds obtained in Examples 11 to 15 were 21.1% at the dosis of 0.3 mg/kg,. . .

DETD TABLE 1

Example	Promoting rate (%) of ***stomach*** excretion at 3 mg/kg (p.o.)	prevention of vomiting in dog at 0.1 mg/kg (s.c.)
1	42	no
2	37	no
3	36	no
4. . .		

DETD TABLE 2

Example	stereo-specf. struct.	Promoting rate (%) of *stomach* excretion in mouse at 3 mg/kg (p.o.)	prevention of vomiting in dog at 0.1 mg/kg (s.c.)
11	2'S,4'S	42.8	no
16	2'R,4'R	20.0	no
17	2'S,4'R	10.6	no
18	2'R,4'S	22.3	no

Stomach excretion activities of Metoclopramide and Cisapride in mouse are as follows:

Metoclopramide	0.3 mg/kg	8.3%
	1.0	9.4
	3.0	25.0
	10.0	34.8
	30.0. . .	

CLM What is claimed is:

4. A pharmaceutical composition comprising an effective amount for promoting activities of the *gastrointestinal tract* of derivative of the formula: ##STR10## or its acid addition salt, in which R.sub.1 is hydrogen atom, lower alkyl, halogen. . .

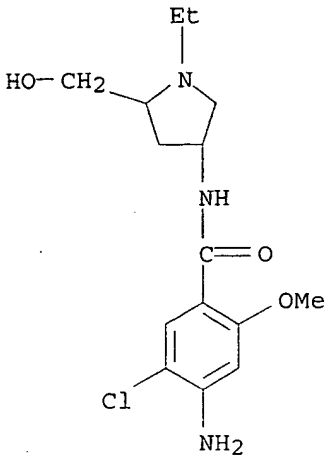
5. A method for promoting activity of the *gastrointestinal tract* which comprises administering an effective amount of a benzamide derivative as defined in claim 1.

IT *142228-16-8P 142228-17-9P 142228-18-0P*
142228-19-1P 142228-20-4P 142228-21-5P
142347-67-9P 142347-68-0P 142347-69-1P
142347-70-4P 142347-71-5P 142347-72-6P
142347-73-7P 142347-74-8P 142347-75-9P
142347-76-0P 142347-77-1P 142347-78-2P
142347-79-3P 142347-80-6P
(preparation of, as gastric motility promoter)

IT *142228-16-8P 142228-17-9P 142228-18-0P*
142228-19-1P 142228-20-4P 142228-21-5P
142347-67-9P 142347-68-0P 142347-69-1P
142347-70-4P 142347-71-5P 142347-72-6P
142347-73-7P 142347-74-8P 142347-75-9P
142347-76-0P 142347-77-1P 142347-78-2P
142347-79-3P 142347-80-6P
(preparation of, as gastric motility promoter)

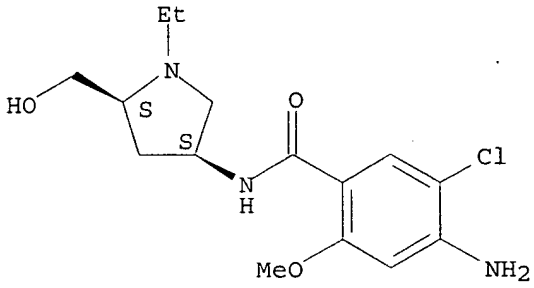
RN 142228-16-8 USPATFULL

CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)



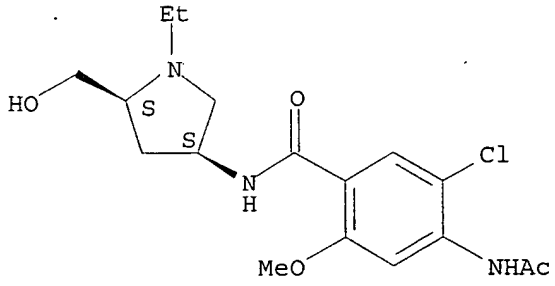
RN 142228-17-9 USPATFULL
CN Benzamide, 4-amino-5-chloro-N-[(3S,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



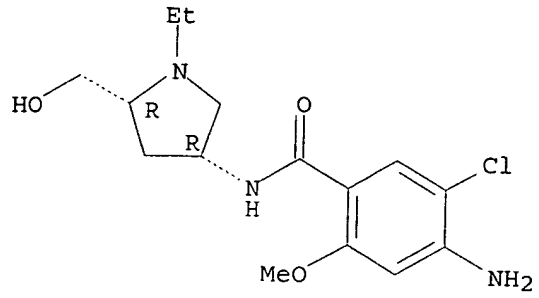
RN 142228-18-0 USPATFULL
CN Benzamide, 4-(acetylamino)-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, (3S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



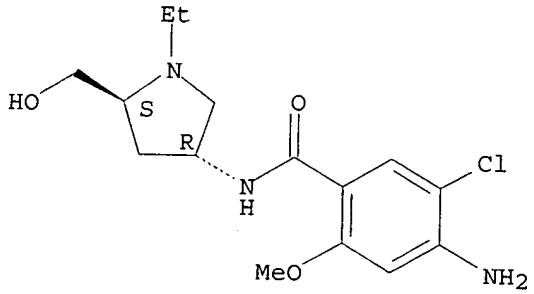
RN 142228-19-1 USPATFULL
CN Benzamide, 4-amino-5-chloro-N-[(3R,5R)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



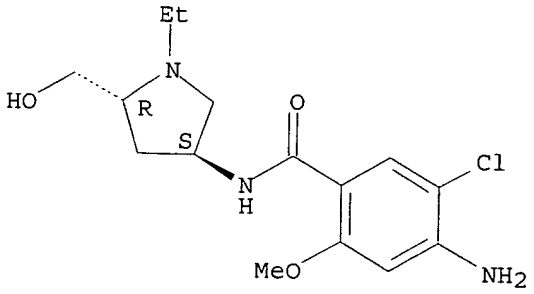
RN 142228-20-4 USPATFULL
CN Benzamide, 4-amino-5-chloro-N-[(3R,5S)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

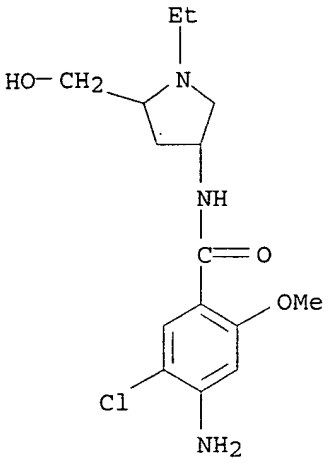


RN 142228-21-5 USPATFULL
CN Benzamide, 4-amino-5-chloro-N-[(3S,5R)-1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

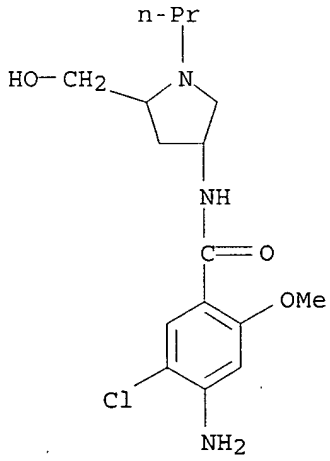


RN 142347-67-9 USPATFULL
CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



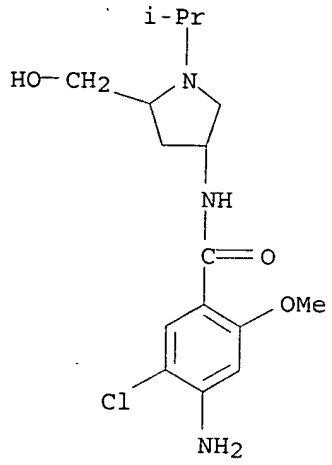
● HCl

RN 142347-68-0 USPATFULL
CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-1-propyl-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



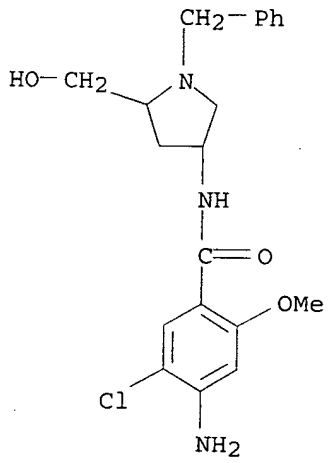
● HCl

RN 142347-69-1 USPATFULL
CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-1-(1-methylethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



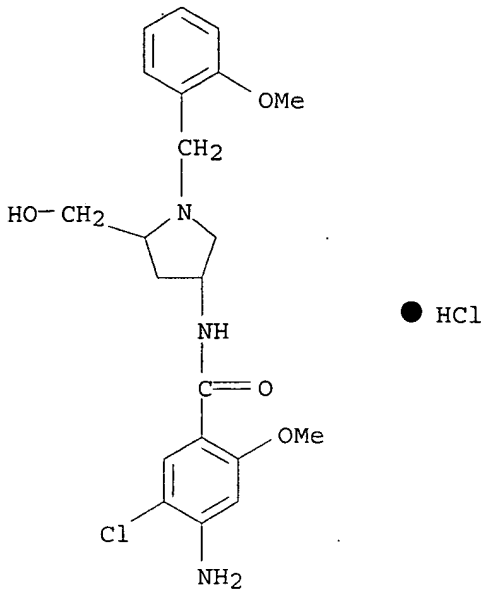
● HCl

RN 142347-70-4 USPATFULL
CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-1-(phenylmethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)

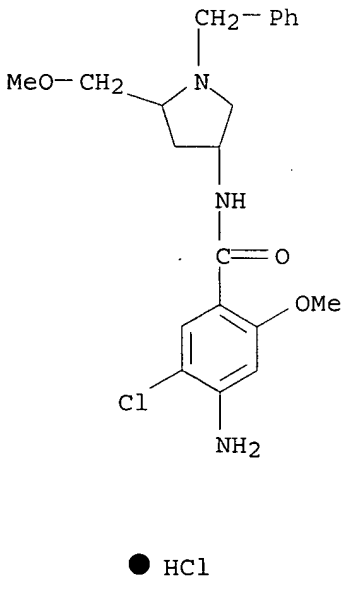


● HCl

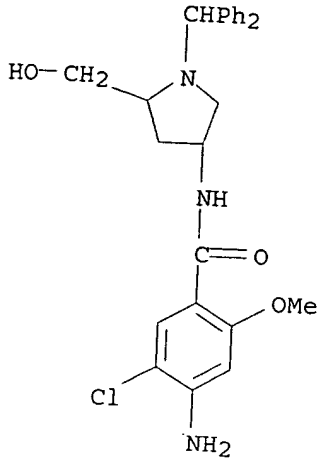
RN 142347-71-5 USPATFULL
CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-1-[(2-methoxyphenyl)methyl]-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



RN 142347-72-6 USPATFULL
CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[5-(methoxymethyl)-1-(phenylmethyl)-3-pyrrolidinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

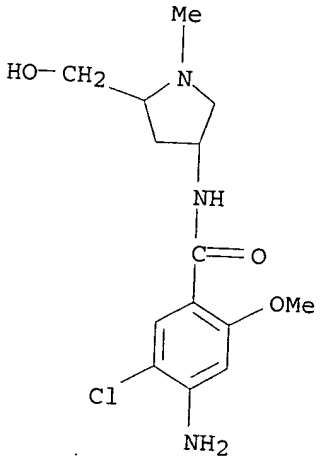


RN 142347-73-7 USPATFULL
CN Benzamide, 4-amino-5-chloro-N-[1-(diphenylmethyl)-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



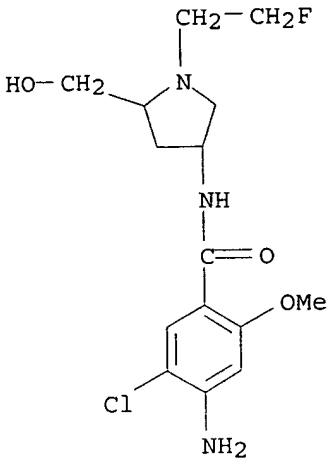
● HCl

RN 142347-74-8 USPATFULL
CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-1-methyl-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



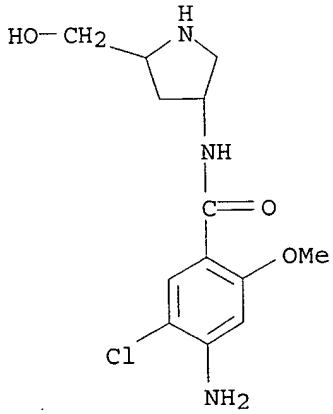
● HCl

RN 142347-75-9 USPATFULL
CN Benzamide, 4-amino-5-chloro-N-[1-(2-fluoroethyl)-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

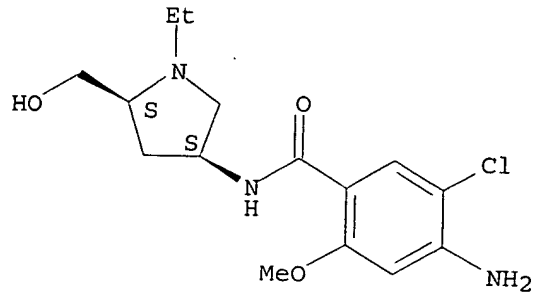
RN 142347-76-0 USPATFULL
CN Benzamide, 4-amino-5-chloro-N-[5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 142347-77-1 USPATFULL
CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride, (3S-cis)- (9CI) (CA INDEX NAME)

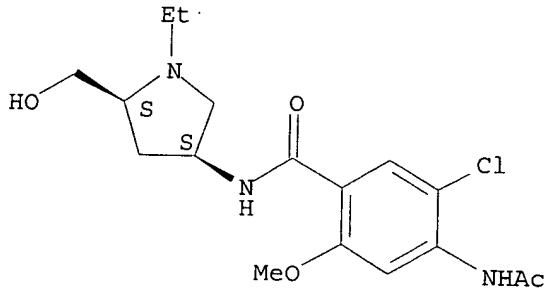
Absolute stereochemistry.



● HCl

RN 142347-78-2 USPATFULL
CN Benzamide, 4-(acetylamino)-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride, (3S-cis)- (9CI) (CA INDEX NAME)

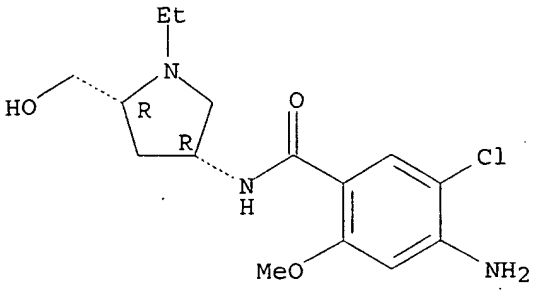
Absolute stereochemistry.



● HCl

RN 142347-79-3 USPATFULL
CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride, (3R-cis)- (9CI) (CA INDEX NAME)

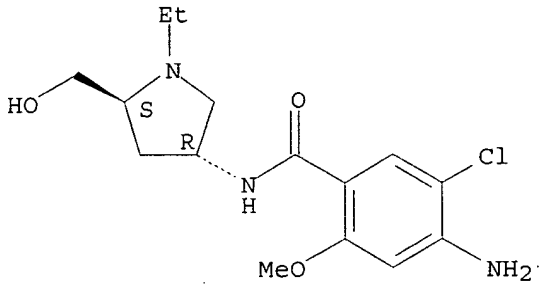
Absolute stereochemistry.



● HCl

RN 142347-80-6 USPATFULL
CN Benzamide, 4-amino-5-chloro-N-[1-ethyl-5-(hydroxymethyl)-3-pyrrolidinyl]-2-methoxy-, monohydrochloride, (3R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

```
=> d his full

     (FILE 'HOME' ENTERED AT 12:40:28 ON 26 OCT 2006)

     FILE 'CAPLUS' ENTERED AT 12:40:34 ON 26 OCT 2006
                E US2005-526780/APPS
L1            1 SEA ABB=ON  PLU=ON  US2005-526780/AP
                D SCA
                SEL RN

     FILE 'REGISTRY' ENTERED AT 12:41:00 ON 26 OCT 2006
L2            9 SEA ABB=ON  PLU=ON  (24201-13-6/BI OR 33996-28-0/BI OR
                33996-30-4/BI OR 672285-79-9/BI OR 672285-80-2/BI OR 672285-81-
                3/BI OR 672285-82-4/BI OR 672285-83-5/BI OR 672285-84-6/BI)
                D SCA

     FILE 'STNGUIDE' ENTERED AT 12:44:26 ON 26 OCT 2006

     FILE 'REGISTRY' ENTERED AT 12:53:56 ON 26 OCT 2006
L3              STRUCTURE UPLOADED
L4            4 SEA SSS SAM L3
                D SCA
L5              STRUCTURE UPLOADED
L6            4 SEA SSS SAM L5
L7           47 SEA SSS FUL L5
                SAVE TEMP L7 SPI780STR7L/A

     FILE 'CAPLUS' ENTERED AT 12:59:24 ON 26 OCT 2006
L8           18 SEA ABB=ON  PLU=ON  L7
L9            1 SEA ABB=ON  PLU=ON  L8 AND L1
                D SCA
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 13:01:16 ON 26 OCT 2006
L10           2 SEA ABB=ON  PLU=ON  (672285-79-9/BI OR 672285-84-6/BI)

     FILE 'REGISTRY' ENTERED AT 13:01:41 ON 26 OCT 2006
                D IDE L10 1-2

     FILE 'CAPLUS' ENTERED AT 13:03:06 ON 26 OCT 2006
                D SCA L8
L11      105205 SEA ABB=ON  PLU=ON  ?STOMACH?/BI
L12       42051 SEA ABB=ON  PLU=ON  ?MOTIL?/BI
L13        4188 SEA ABB=ON  PLU=ON  ?PERISTAL?/BI
L14      249583 SEA ABB=ON  PLU=ON  ?DIGEST?/BI
L*** DEL 199220 S ?INTESTIN?
L15      288318 SEA ABB=ON  PLU=ON  ?INTESTIN?/BI
L16       43191 SEA ABB=ON  PLU=ON  (5HT OR 5 HT?)/BI
L17       77545 SEA ABB=ON  PLU=ON  ?SEROTONIN?/BI
L18       22550 SEA ABB=ON  PLU=ON  ?ILEUM?/BI
L19       18576 SEA ABB=ON  PLU=ON  ?JEJUN?/BI
L20       31539 SEA ABB=ON  PLU=ON  ?DUODEN?/BI
L21      139482 SEA ABB=ON  PLU=ON  TRACT#/BI
L22      171670 SEA ABB=ON  PLU=ON  ?GASTR?/BI
L23          12 SEA ABB=ON  PLU=ON  L8 AND (L11 OR L12 OR L13 OR L14 OR L15 OR
                L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22)
L24         162 SEA ABB=ON  PLU=ON  KITAJIMA A?/AU
L25           3 SEA ABB=ON  PLU=ON  AKIHIKO K?/AU
L26           5 SEA ABB=ON  PLU=ON  KAMODA O?/AU
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L27          22 SEA ABB=ON  PLU=ON  OSAMU K?/AU
                E KAMODA/AU
L28           6 SEA ABB=ON  PLU=ON  OHSAKO A?/AU
L29           2 SEA ABB=ON  PLU=ON  AKIHIRO O?/AU
L30         574 SEA ABB=ON  PLU=ON  YANAGI T?/AU
L31           1 SEA ABB=ON  PLU=ON  TOSHIHARU Y?/AU
L32         165 SEA ABB=ON  PLU=ON  (L24 OR L25)
L33          27 SEA ABB=ON  PLU=ON  (L26 OR L27)
L34           8 SEA ABB=ON  PLU=ON  (L28 OR L29)
L35         575 SEA ABB=ON  PLU=ON  (L30 OR L31)
L36           1 SEA ABB=ON  PLU=ON  L32 AND (L33 OR L34 OR L35)
L37           5 SEA ABB=ON  PLU=ON  L33 AND (L34 OR L35)
L38           1 SEA ABB=ON  PLU=ON  L34 AND L35
L39           5 SEA ABB=ON  PLU=ON  (L36 OR L37 OR L38)
L40           3 SEA ABB=ON  PLU=ON  (L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR
                L30 OR L31) AND (L23 OR L8)

     FILE 'MEDLINE' ENTERED AT 13:14:46 ON 26 OCT 2006
L41         235 SEA ABB=ON  PLU=ON  (L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR
                L30 OR L31)
L42           2 SEA ABB=ON  PLU=ON  (L36 OR L37 OR L38)

     FILE 'REGISTRY' ENTERED AT 13:16:02 ON 26 OCT 2006
                SET SMARTSELECT ON
L43             SEL PLU=ON  L7 1- CHEM :      49 TERMS
                SET SMARTSELECT OFF

     FILE 'MEDLINE' ENTERED AT 13:16:05 ON 26 OCT 2006
L44           3 SEA ABB=ON  PLU=ON  L43
                D SCA
                D TRIAL 1-3
                D QUE L44
                D L43
                D L43 1-49
L45           0 SEA ABB=ON  PLU=ON  FAUC65
L46           5 SEA ABB=ON  PLU=ON  TKS159
                D TRIAL 1-5
L47     1149902 SEA ABB=ON  PLU=ON  (L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR
                L17 OR L18 OR L19 OR L20 OR L21 OR L22)
L48           5 SEA ABB=ON  PLU=ON  L47 AND ((L44 OR L45 OR L46))
L49           2 SEA ABB=ON  PLU=ON  L41 AND (L44 OR L46 OR L48)

     FILE 'EMBASE' ENTERED AT 13:20:17 ON 26 OCT 2006
L50         198 SEA ABB=ON  PLU=ON  (L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR
                L30 OR L31)
L51           2 SEA ABB=ON  PLU=ON  (L36 OR L37 OR L38)

     FILE 'REGISTRY' ENTERED AT 13:20:54 ON 26 OCT 2006
                SET SMARTSELECT ON
L52             SEL PLU=ON  L7 1- CHEM :      49 TERMS
                SET SMARTSELECT OFF

     FILE 'EMBASE' ENTERED AT 13:20:56 ON 26 OCT 2006
L53           7 SEA ABB=ON  PLU=ON  L52
L54           4 SEA ABB=ON  PLU=ON  FAUC65 OR TKS159
L55           7 SEA ABB=ON  PLU=ON  (L53 OR L54)
L56           7 SEA ABB=ON  PLU=ON  (L53 OR L54) AND (L11 OR L12 OR L13 OR L14
                OR L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22)
                D TRIAL 1-7
L57           2 SEA ABB=ON  PLU=ON  L50 AND (L53 OR L54 OR L56)
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     FILE 'BIOSIS' ENTERED AT 13:25:28 ON 26 OCT 2006
L58          252 SEA ABB=ON  PLU=ON  (L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR
                 L30 OR L31)
L59            4 SEA ABB=ON  PLU=ON  (L36 OR L37 OR L38)

     FILE 'REGISTRY' ENTERED AT 13:25:56 ON 26 OCT 2006
                 SET SMARTSELECT ON
L60              SEL PLU=ON  L7 1- CHEM :       49 TERMS
                 SET SMARTSELECT OFF

     FILE 'BIOSIS' ENTERED AT 13:25:57 ON 26 OCT 2006
L61            3 SEA ABB=ON  PLU=ON  L60
L62            5 SEA ABB=ON  PLU=ON  FAUC65 OR TKS159
L63            2 SEA ABB=ON  PLU=ON  L58 AND (L61 OR L62)

     FILE 'REGISTRY' ENTERED AT 13:27:39 ON 26 OCT 2006
L64            1 SEA ABB=ON  PLU=ON  FAUC 65/CN
L65            1 SEA ABB=ON  PLU=ON  TKS 159/CN
                 D SCA
                 D SCA L64
                 SEL RN L10
                 SEL RN L64
                 SEL RN L65
L66            1 SEA ABB=ON  PLU=ON  (672285-79-9/CRN OR 672285-84-6/CRN OR
                 627529-76-4/CRN OR 142228-17-9/CRN)
                 D SCA
                 D IDE L64
                 D IDE L65
                 D IDE L66
                 D STAT QUE L7
L67            4 SEA ABB=ON  PLU=ON  L65 OR L66 OR L10
                 D SCA

     FILE 'USPATFULL, USPAT2' ENTERED AT 13:39:42 ON 26 OCT 2006
L68            3 SEA ABB=ON  PLU=ON  L67
                 D SCA
L69            4 SEA ABB=ON  PLU=ON  L7
L70       308291 SEA ABB=ON  PLU=ON  (L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR
                 L17 OR L18 OR L19 OR L20 OR L21 OR L22)
L71            3 SEA ABB=ON  PLU=ON  L69 AND L70
L72          183 SEA ABB=ON  PLU=ON  L41
L73            7 SEA ABB=ON  PLU=ON  L42
L74            1 SEA ABB=ON  PLU=ON  L72 AND (L69 OR L71)

     FILE 'STNGUIDE' ENTERED AT 13:42:37 ON 26 OCT 2006

     FILE 'REGISTRY' ENTERED AT 13:45:53 ON 26 OCT 2006
                 D STAT QUE L7

     FILE 'CAPLUS' ENTERED AT 13:45:54 ON 26 OCT 2006
                 D QUE NOS L39
                 D QUE NOS L40
L75            6 SEA ABB=ON  PLU=ON  L39 OR L40

     FILE 'MEDLINE' ENTERED AT 13:45:58 ON 26 OCT 2006
                 D QUE NOS L42
                 D QUE NOS L49
L76            3 SEA ABB=ON  PLU=ON  L42 OR L49
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     FILE 'EMBASE' ENTERED AT 13:46:01 ON 26 OCT 2006
                D QUE NOS L51
                D QUE NOS L57
L77           3 SEA ABB=ON  PLU=ON  L51 OR L57

     FILE 'BIOSIS' ENTERED AT 13:46:04 ON 26 OCT 2006
                D QUE NOS L59
                D QUE NOS L63
L78           5 SEA ABB=ON  PLU=ON  L59 OR L63

     FILE 'USPATFULL, USPAT2' ENTERED AT 13:46:07 ON 26 OCT 2006
                D QUE NOS L73
                D QUE NOS L74
L79           7 SEA ABB=ON  PLU=ON  L73 OR L74

     FILE 'STNGUIDE' ENTERED AT 13:46:29 ON 26 OCT 2006

     FILE 'CAPLUS, MEDLINE, EMBASE, BIOSIS, USPATFULL, USPAT2' ENTERED AT
     13:46:50 ON 26 OCT 2006
L80          12 DUP REM L75 L76 L77 L78 L79 (12 DUPLICATES REMOVED)
                       ANSWERS '1-6' FROM FILE CAPLUS
                       ANSWERS '7-9' FROM FILE BIOSIS
                       ANSWERS '10-12' FROM FILE USPATFULL
                  D IBIB ABS HITIND HITSTR L80 1-6
                  D IALL L80 7-9
                  D IBIB ABS KWIC HITSTR L80 10-12

     FILE 'REGISTRY' ENTERED AT 13:51:05 ON 26 OCT 2006
                D STAT QUE L7

     FILE 'CAPLUS' ENTERED AT 13:51:07 ON 26 OCT 2006
                D QUE NOS L8
                D QUE NOS L23
L81          15 SEA ABB=ON  PLU=ON  (L8 OR L23) NOT L75

     FILE 'MEDLINE' ENTERED AT 13:51:10 ON 26 OCT 2006
                D QUE NOS L44
                D QUE NOS L46
                D QUE NOS L48
L82           3 SEA ABB=ON  PLU=ON  (L44 OR L46 OR L48) NOT L76

     FILE 'EMBASE' ENTERED AT 13:51:14 ON 26 OCT 2006
                D QUE NOS L53
                D QUE NOS L54
                D QUE NOS L56
L83           5 SEA ABB=ON  PLU=ON  (L53 OR L54 OR L56) NOT L77

     FILE 'BIOSIS' ENTERED AT 13:51:18 ON 26 OCT 2006
                D QUE NOS L61
                D QUE NOS L62
L84           3 SEA ABB=ON  PLU=ON  (L61 OR L62) NOT L78

     FILE 'USPATFULL, USPAT2' ENTERED AT 13:51:21 ON 26 OCT 2006
                D QUE NOS L69
                D QUE NOS L71
L85           3 SEA ABB=ON  PLU=ON  (L69 OR L71) NOT L79

     FILE 'CAPLUS, MEDLINE, EMBASE, BIOSIS, USPATFULL' ENTERED AT 13:53:56 ON
     26 OCT 2006
L86          22 DUP REM L81 L82 L83 L84 L85 (7 DUPLICATES REMOVED)
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ANSWERS '1-15' FROM FILE CAPLUS
ANSWER '16' FROM FILE MEDLINE
ANSWERS '17-18' FROM FILE EMBASE
ANSWER '19' FROM FILE BIOSIS
ANSWERS '20-22' FROM FILE USPATFULL
D IBIB ABS HITIND HITSTR L86 1-15
D IALL L86 16-19
D IBIB ABS KWIC HITSTR L86 20-22

FILE HOME

FILE CAPLUS

FILE COVERS 1907 - 26 Oct 2006 VOL 145 ISS 18
FILE LAST UPDATED: 25 Oct 2006 (20061025/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 25 OCT 2006 HIGHEST RN 911284-77-0
DICTIONARY FILE UPDATES: 25 OCT 2006 HIGHEST RN 911284-77-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE STNGUIDE
FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Oct 25, 2006 (20061025/UP).

FILE MEDLINE
FILE LAST UPDATED: 25 Oct 2006 (20061025/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE EMBASE
FILE COVERS 1974 TO 26 Oct 2006 (20061026/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 18 October 2006 (20061018/ED)

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 26 Oct 2006 (20061026/PD)
FILE LAST UPDATED: 26 Oct 2006 (20061026/ED)
HIGHEST GRANTED PATENT NUMBER: US7127745
HIGHEST APPLICATION PUBLICATION NUMBER: US2006242744
CA INDEXING IS CURRENT THROUGH 24 Oct 2006 (20061024/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 26 Oct 2006 (20061026/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2006

FILE USPAT2

FILE COVERS 2001 TO PUBLICATION DATE: 26 Oct 2006 (20061026/PD)
FILE LAST UPDATED: 26 Oct 2006 (20061026/ED)
HIGHEST GRANTED PATENT NUMBER: US2006139723
HIGHEST APPLICATION PUBLICATION NUMBER: US2006242346
CA INDEXING IS CURRENT THROUGH 26 Oct 2006 (20061026/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 26 Oct 2006 (20061026/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2006